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The Lyophilic Colloids

(Their Theory and Practice)

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TO

WOLFGANG OSTWALD

FOR BRINGING ORDER OUT OF CHAOS

AND LIGHT INTO THE NIGHT

If such things be purged as ought to be purged, they are profitable; otherwise it falls out contrary.—HIPPOCRATES.

PREFACE

This volume summarizes our work of the last fifteen years. It has as its purpose the restatement of a theory of the lyophilic colloid then proposed but fortified in these pages by observations which seem to make it binding. Our interest was and continues to be in living matter; but to say that living matter is a lyophilic colloid system does not tell us anything of the nature of the lyophilic colloid itself. We have, apparently, arrived at an answer to this chemically and physically more fundamental problem. We were not anxious to enter the field of either the chemist or the physicist, but it seems to be the fate of biological workers and colloid chemists that they must. The succeeding pages will help to explain, we hope, why biologists have not been able to rediscover, ready-made, in living matter the laws particularly of the physical chemists; and also why another point of view is due in chemistry if we would understand a host of problems of the existence of which, but not of the solution of which, the workers in pure or applied chemistry have long been cognizant.

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JULY 1933

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THE GENERAL NATURE OF THE LYOPHILIC COLLOID

PART ONE

THE GENERAL NATURE OF THE LYOPHILIC COLLOID

I. Historical Remarks

Since the recognition of the colloids by Thomas Graham[1] as a "new world of matter," the most fundamental contribution to our knowledge of these systems is their classification by Wolfgang Ostwald.[2] Since then colloids have ceased to be substances and have become materials in a given state. His studies have shown all colloid systems to be dispersed systems (or dispersoids), these differing from the molecularly dispersed systems to which the chemist has fairly exclusively limited his interests or the coarsely dispersed of the physicist only in the matter of the size of the subdivided particles—colloid systems lie between the two, the particles of the subdivided material being larger than molecular (more than 1 μμ) and still not so coarse as to fall within the ranges of easy measurement and the laws of the physicist (less than 0.1 μ). While these numerical limits are somewhat arbitrary in that transition from coarse suspensions to colloid "solutions" and transition from these to the "true" solutions of the chemist does not occur suddenly but only gradually, nevertheless, the fundamental definition of the colloids as dispersoids possessed of a limited degree of subdivision remains.

Ostwald was also the first to recognize that the "colloid solutions" of his day (subdivisions, for the most part, of solid materials in a liquid of some sort) constituted only one class of the possible dispersoids of nature. From the three states of matter of the physicist it is obvious that nine mixtures may be made, any of which will be a "colloid" if the dimensions of the

[1] Thomas Graham: Phil. Trans. 183 (1861); Liebig's Annalen *121*, 13 (1862).

[2] Wolfgang Ostwald: Kolloid-Zeitschr. *1*, 291 and 331 (1907); his views are formulated in running form in his classic texts of colloid chemistry, An Introduction to Theoretical and Applied Colloid Chemistry, 2nd Am. Ed. Trans. by Fischer, New York (1922); A Handbook of Colloid Chemistry, 2nd Eng. Ed. Trans. by Fischer, Philadelphia (1919).

materials divided within the dispersion medium are the proper ones. On this basis OSTWALD constructed the following table:

Gas in gas	Gas in liquid	Gas in solid
Liquid in gas	Liquid in liquid	Liquid in solid
Solid in gas	Solid in liquid	Solid in solid

Since gases are presumed to be in a state of molecular subdivision or even finer, it is obvious that gas in gas dispersions can never attain colloid dimensions. Out of the nine possible mixtures, only eight are therefore realizable (and have been realized) by the colloid chemist. Steam, smoke, foam, fine emulsions, fine suspensions, tufa, inclusion waters, certain precious stones—these are common representatives of the eight remaining classes as listed above.

The utilization of this concept of the colloids contributed much to the understanding of these systems, not only in bringing an interpretation of what workers in colloid chemistry had discovered before it was advanced, but in furnishing the theoretical foundation upon which new discoveries might build. Thus the conditions necessary for the production or the destruction of colloid systems became formulated as laws (they can be produced only through the *condensation* of molecularly dispersed systems or through the finer *dispersion* of more coarsely aggregated systems), while changes within the colloids themselves (as their changes in viscosity, in optical, electrical and other properties) were made comprehensible on the basis of change merely in the size of the dispersed particles.

Within the total realm of the colloids there was early distinguished, however, by A. A. NOYES,[3] the existence of two well-defined groups; on the one hand, those "non-viscid, non-gelatinizing and easily precipitated by salts"; on the other, those "viscid, gelatinizing and not easily precipitated by salts." NOYES called the former (of which gold or silver in water is a common example) the "colloid suspensions," the latter (of which gelatin in water is the standard illustration) the "colloid solutions." Since PERRIN'S[4] studies of the subject, we call the former the hydrophobic colloids, the latter the hydrophilic; or we use the more

[3] A. A. NOYES: Jour. Am. Chem. Soc. *27*, 85 (1905).

[4] J. PERRIN: Journal de Chimie Physique, *3*, 84 (1905).

generic terminology of FREUNDLICH[5] and call them lyophobic and lyophilic—solvent-hating and solvent-loving.

The physiologist or physiological chemist deals almost exclusively with colloids lyophilic in type. But an enormous fraction of industrial chemistry is also of this category as witness the manufacture of glues, pastes, soaps, food products, many dyes, lubricating greases, rubber and cement. It is only the laboratory chemist who has much to do with the typical lyophobic colloids. And yet it is the theoretical deductions which have been derived from the study of these systems that have been utilized in largest measure for an understanding of that practically larger and more important group of the lyophilic colloids. How inadequate are these deductions is familiar to every worker in the lyophilic realm.

Since the appearance of a recent critical review of the theories of the lyophilic colloid by WOLFGANG OSTWALD,[6] it is not necessary to rediscuss the matter here. We shall, in consequence, pass at once to a restatement of that theory which we proposed some years ago,[7] utilizing the succeeding pages for the adduction of various proofs for the correctness of this notion and to indicate the corollaries in pure and applied chemistry which follow from it.

II. A GENERAL THEORY OF THE LYOPHILIC COLLOID

The light metal soaps with water or a large number of other "solvents" yield lyophilic colloid systems peculiarly well adapted to any study of the properties of such systems and their fundamental nature.[8] The fatty acids are chemically well-defined compounds, they may be obtained in pure form and the production of "soaps" from them through the introduction of different bases is easy.

The "solvents" with which such soaps may be mixed to yield typical lyophilic colloids are large in number and they are so

[5] H. FREUNDLICH: Kolloid-Zeitschr. *3*, 80 (1908); Kappillarchemie, 309, Leipzig (1909).

[6] WOLFGANG OSTWALD: Kolloid-Zeitschr. *46*, 248 (1928).

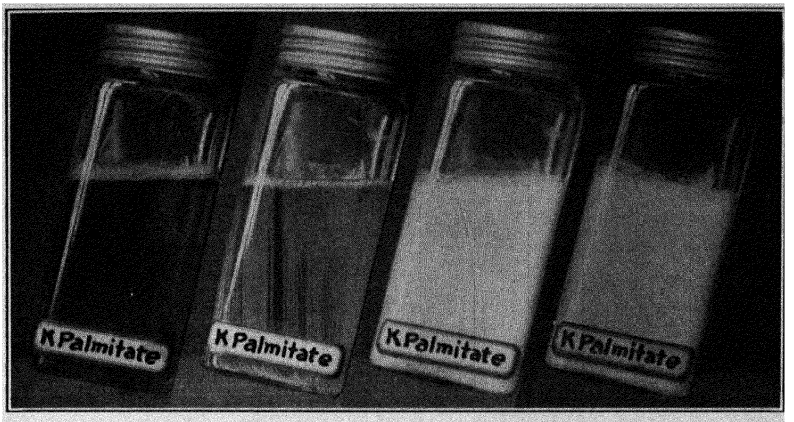
[7] MARTIN H. FISCHER and MARIAN O. HOOKER: Science, *48*, 143 (1918); *ibid.*, *49*, 615 (1919); Chemical Engineer, *27*, 184 (1919); Soaps and Proteins, 69, New York (1921).

[8] See MARTIN H. FISCHER: Soaps and Proteins, New York (1921).

various that they run the gamut from the electrolytically active water on the one hand, to the chemically "dead" paraffins on the other.

Any sodium, potassium, lithium or ammonium soap of the commoner fatty acids yields an equally good lyophilic colloid system with either water or alcohol (and many other "solvents"). What happens when a twenty-five per cent mixture of potassium palmitate with water or alcohol is heated to 100° C. in a water bath and is then allowed to chill is shown in Fig. 1. At the higher temperatures (above 85° C.) the mixture with either of these solvents yields a water-like solution (bottle *a* of Fig. 1). The solution thus produced is not only optically clear but boils at a point little above the boiling point of the water or the alcohol used—it is, in other words, a true (molecular) solution at this temperature. When permitted to cool (say to 40° C.) these solutions first become opalescent (*b* of Fig. 1), then milky (say at 20° C. as shown in bottle *c* of Fig. 1), progressively more viscid and finally set into a fairly solid gel (say at 5° C. as shown in bottle *d* of Fig. 1). Here without changes in the chemical concentration of the whole system and without large changes even in the matter of temperature, a given mixture changes from the chemist's ideal solution to the most typical product of the colloid chemical laboratory.

What we believe happens, not only in this illustration but in all lyophilic colloid systems, is represented by the diagrams *A* and *B* of Fig. 2. Diagram *A* is representative of systems in which the two phases are liquid at the temperatures employed, diagram *B* when the separating phase is solid or crystalline. If, for illustration, the system soap/water is chosen (say, 25 per cent potassium oleate/water in illustration of diagram *A* and 25 per cent sodium stearate/water in illustration of diagram *B*) the entire set of systems illustrated in the two diagrams may be obtained through mere change in temperature. At higher temperatures, the soap "dissolves" *in* the water and there results a "true" solution. This matter is represented by the region marked *A* in the diagrams (the soap is dispersed molecularly or ionically *in* the solvent). As the temperature is *lowered,* the solubility of the soap in the water is decreased and as the saturation point for the lower temperature is attained, the soap par-



a *b* *c* *d*

FIG. 1

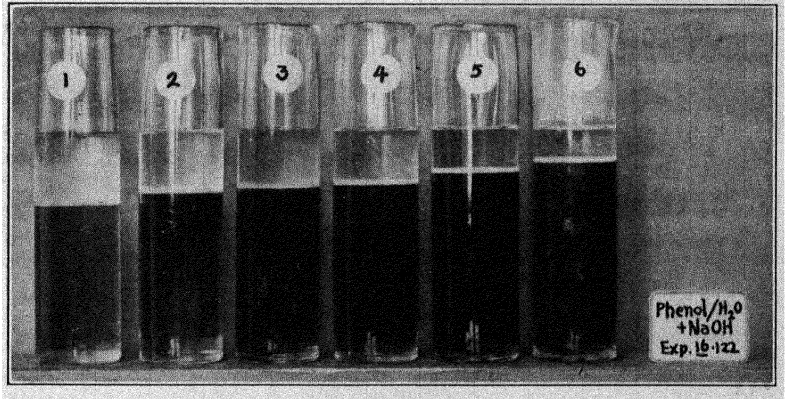
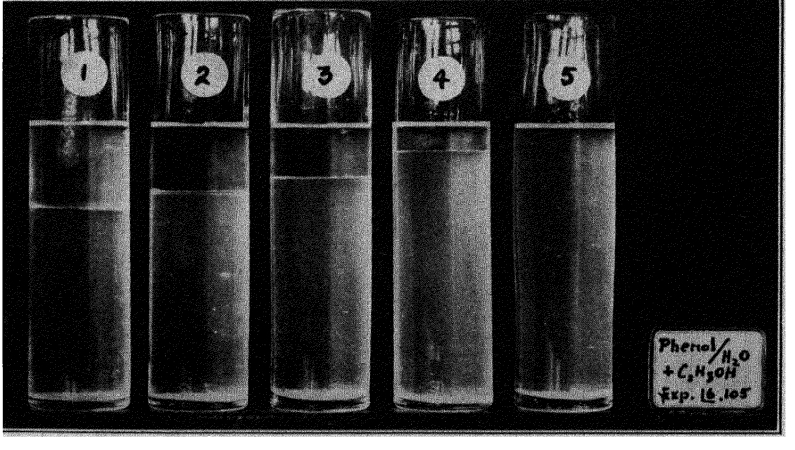


FIG. 3



ticles must obviously assume more than molecular size. By definition, therefore, we approach with falling temperature the realm of the colloids, or that of dispersions of one material in a second with the degree of dispersion showing dimensions greater than the molecular. This gradual increase in the size of the soap particles (or increase in their number) with lowering of the temperature is represented by the regions *B, C, D, E* and *F*.

Such supersaturation with agglomeration of particles, while yielding us a colloid system, does not yet tell us whether it will be lyophobic or lyophilic (or, depending upon the liquid or solid nature of the separating phase, an emulsion or a suspension colloid). *The lyophobic colloid results when the solvent is not soluble, the lyophilic when the solvent is soluble in the precipitating phase.* When soap falls out of solution from such a solvent as allyl alcohol, the former of these possibilities is satisfied (and we get a lyophobic colloid); when it falls out from most other alcohols or, as in our illustration, from water, the latter is satisfied (and we get a lyophilic "sol" or "gel"). The black circles or crystal clusters in the diagrams of Fig. 2 represent more, therefore, in the latter instance than precipitates of pure soap; they are this, plus a certain amount of the water (or other "solvent") dissolved in them.

At a sufficiently low temperature the soap aggregates will have become so large or so numerous as to touch and coalesce. This process continued sufficiently must yield ultimately a single system in which the soap has now become the "solvent" *for* the water. Diagrammatically this situation is represented by the zone *Z* of Fig. 2.

Between the upper extreme *A* of a solution of the soap in the solvent and the lower extreme *Z* of the solvent in the soap, there exist two main zones of mixed systems—one below the upper (*B, C, D* and *E*) consisting of a dispersion of solvated-soap in the soaped-solvent, and a second above the lower (*Y, X, W* and *V*) consisting of soaped-solvent in the solvated-soap. These two mixed systems (if the soap is liquid) are in essence emulsions, but of opposite type and as such (even when of the same *quantitative* chemical constitution) are possessed of totally different physical properties. The former corresponds, for example, to an emulsion of oil-in-water, the second to one of water-in-oil, and

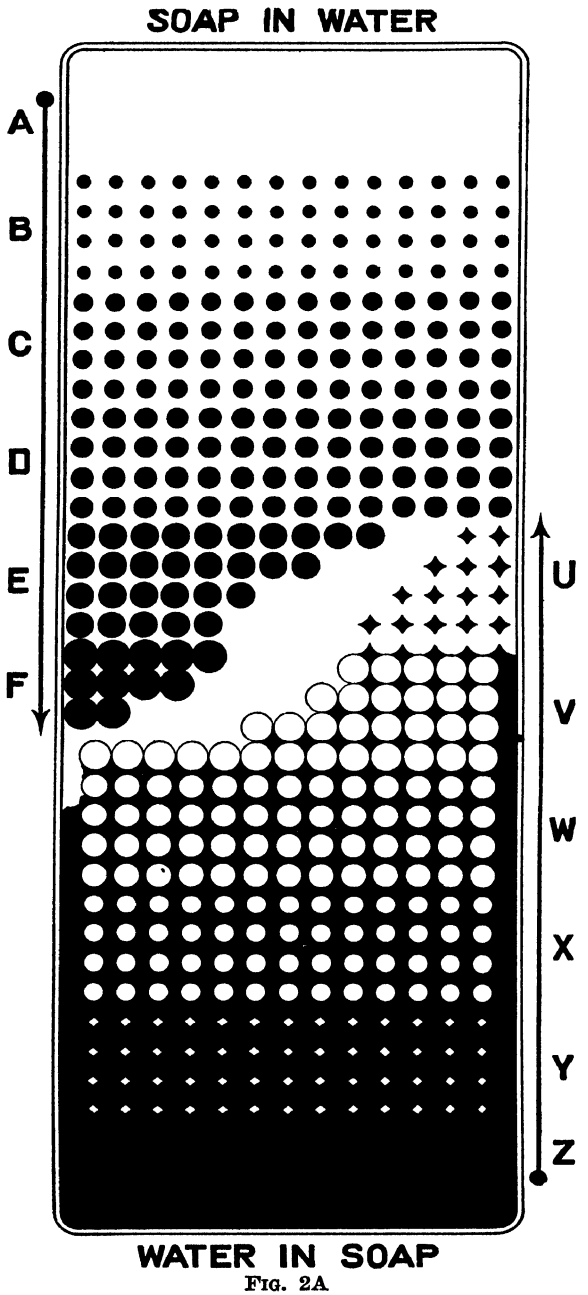


FIG. 2A

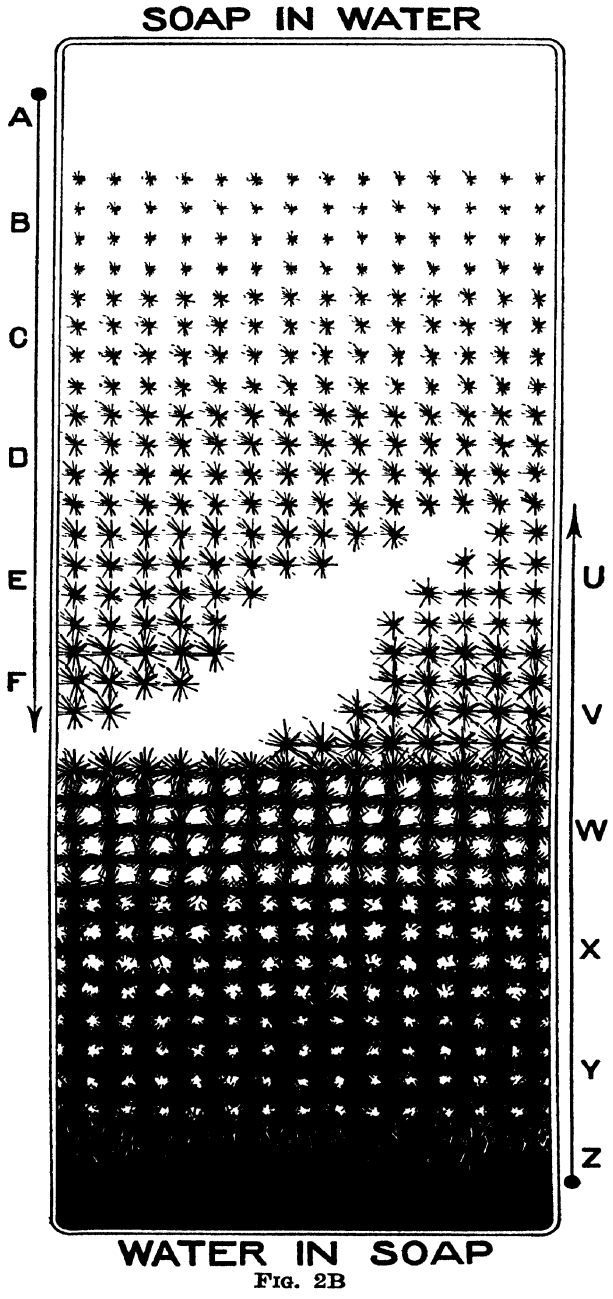


FIG. 2B

as the former (as illustrated by milk) will mix with water, wet paper and show a certain viscosity value, the latter (as illustrated by butter) will mix only with oil, will grease paper and show an entirely different viscosity.[9]

Returning to the lyophilic soap and the diagrams, it is obvious that as we descend, with lowering of temperature, from the region *A*, we pass in the regions *B*, *C* and *D* through increasingly viscid *liquid* colloid "solutions" (so-called sols) but all of them emulsions of the type solvated-soap in soap-water. In the region *E*, the particles of solvated soap almost touch and here the highest (liquid) viscosity is obtained. In *F* they do touch and now form a continuous external phase. At this point we change to the opposite type of emulsion (to one of soap-water in solvated-soap) and the previously liquid colloid becomes solid. As ordinarily put, the mixture *gels*.

III. Some Critical Remarks

We wish now to emphasize how this concept of the changes which a soap/water system suffers in passing from a liquid sol to a dry gel may help to explain some of the "strange" characteristics of colloid systems.

It is clear, first, that this general notion sets no limitations upon the nature of the materials that may go to make up a lyophilic colloid system and makes no specifications as to the nature of the forces which guarantee its stability. They are, in general, any or all the forces which appear or are operative whenever "solution" of any kind occurs.

This is emphasized because there has been much written, for example, regarding the all-important effects of such single elements as the electrical charges, the hydrogen ion concentration, etc., in determining the stability of colloids in general or that of the lyophilic colloids in particular. We do not wish to deny that electrical charges or hydrogen or hydroxyl ions may not sometimes play some rôle in determining the behavior of some colloid systems. It seems quite probable, for example, that electrical notions may explain the stability of a few of the

[9] See in this connection Martin H. Fischer and Marian O. Hooker: Science, *43*, 468 (1916); Kolloid-Zeitschr., *18*, 129 (1916); *ibid.*, *18*, 242 (1916); Fats and Fatty Degeneration, 20, New York (1917).

(lyophobic) colloid metals. But even here the quantitative effects of electrolytes in producing their precipitation, for example, begin to diminish and to show "abnormalities" as soon as the nobler metals (like gold and platinum) are replaced by aluminium, iron, tin or zinc hydroxids (by materials, in other words, which show the beginnings of hydrophilic properties and "solvation" in solution). Such electrical notions are altogether too narrow for any general theory of the lyophilic colloids. While it is true that electrical forces may *appear* in systems composed of soaps and water (or of proteins and water) *they are not the reasons for the existence of such systems.* It is natural that electrical phenomena must appear in these systems whenever the system as a whole has any of the phase, soap- (or protein-) dissolved-in-water present in it, in other words, in all the regions of our diagrams above the level *Y*. But the discoverable electrical charges or the hydrogen or hydroxyl ion concentrations no more determine the properties of such colloid systems than the H or OH ions of distilled water explain its physical state; the electrical charges and the hydrogen and hydroxyl ion concentrations are only the accidental consequences of the fact that one of the components of the colloid system (soap or protein) is "soluble," hydrolyzable and ionizable in any excess of (uncombined) water that may be present. That the electrical phenomena are an accidental consequence, and not a cause of the behavior of such colloid systems, is proved by the fact that soaps form as good or better colloid systems with the most varied types of "organic" solvents (as the anhydrous alcohols, toluene, benzene, chloroform or ether).[10] And where are the electrical forces when lyophilic colloid systems are built up of nitrocellulose with ether and alcohol, agar-agar with water, or rubber with benzene? What remains are two mutually soluble substances and the forces active are any or all that appear whenever such mutual "solution" occurs.

The two diagrams also emphasize the existence of two types of systems which have largely escaped notice, namely, those that lie *below* the level *F*. Colloid systems have been regarded almost exclusively as dispersions of *a* in *b* (as non-solvated or solvated particles *in* the dispersion medium). But the regions *W*, *X*

[10] See page 164.

and *Y* show the existence of dispersions of *b* in *a* (varying from coarser dispersions of the dispersion medium within the solvated mass to the final molecular solution of the original solvent in the "colloid").

The diagrams serve to clarify also the colloid-chemical concepts of *hysteresis, gelation capacity, swelling and syneresis.* By hysteresis is here meant "lag."

When it is borne in mind that the absolute solubility values of any two mutually soluble substances are rarely the same and that the rates at which they go into solution into each other are usually different, it becomes apparent why the attainment of equilibrium in any such system requires time. Thus, with lowering of temperature, for example, a lyophilic colloid system tends to set generally at a temperature lower than that at which it will liquefy when, upon a reversal of experimental conditions, the temperature is raised. The course of the curve marking the change, say of viscosity or optical heterogeneity, with a falling temperature does not coincide with the curve marking the change in the same properties when the temperature is elevated. We say that the lyophilic colloid retains or "remembers" the state from which it has come. If the conditional change through which the lyophilic colloid system is carried is brought about rapidly, such curves lie far apart; but they tend to become identical if sufficient time is taken. The time factor is necessary for the establishment of equilibrium in the two types of solution.

The point at which a lyophilic colloid system gels is obviously that at which the solvated colloid phase becomes the external one. The colloid system at this point still contains, as an internal phase, a solution of the colloid in the solvent. Gelation capacity is, therefore, always greater than the solvation or hydration capacity of a colloid. The latter measures the solubility of the solvent in the colloid material. The increase in the volume of the latter, as the solvent is taken up, is the measure of its ability to "swell." The zone *Z* in the diagrams covers the swelling capacity of a given material with its "solvent"; the gelation capacity embraces all the zones above this up to and including the zone *V*.

As soon as this zone is passed, the external solvated colloid phase may not be adequate to inclose all the solution of colloid-

in-solvent, at which point the system as a whole tends to sweat, in other words, to show the characteristic phenomenon of syneresis. The failure to inclose adequately the internal phase will be more likely if one of the materials of the mutually soluble system is solid than when both are liquid, wherefore, colloids of the solvated *solid* type (like sodium stearate/water, silicic acid/water) will show a greater degree of syneresis than more liquid ones (like sodium oleate/water, rubber/benzene, etc.).

Finally, this concept of the lyophilic colloid should make clear the reasons for the age-old conflict between those workers in colloid chemistry who have been able to find in colloid systems "nothing but" the laws of the pure chemist and the physical chemist, and those who have not. A colloid chemist who works with colloid systems of low concentration (say a dilute gelatin/water system) works obviously at a level such as indicated by *B*, *C*, or *D* in the diagrams. If a horizontal line is drawn through such a level, it passes for the most part through a dilute solution which will explain why such an observer will note *predominantly* in his system nothing but the characteristics of such a solution. Another chemist working with systems of a higher concentration (say a gelatin gel) is busy at the levels *X*, *Y*, or *Z*. But a horizontal line drawn through these levels encounters little or no dilute solution. He works in fact with one that, in common parlance, is "concentrated," or one which in our language is of inverse type, and as yet but little studied. As the succeeding pages will show, such an one will find his system in no way related to the concepts of solution devised for him by the dilute solution chemists, and so will be inclined to throw them overboard.

IV. Some Characteristics of Mutually Soluble Systems

As soon as it is said that a lyophilic colloid with its dispersion medium (like a soap with its "solvent") constitutes a mutually soluble system, we become interested in mutually soluble systems on their own account. They seem to have received first study by J. Friedländer[11] and V. Rothmund.[12] Even earlier, W. B.

[11] J. Friedländer: Zeitschr. f. physik. Chem., *38*, 430 (1901).

[12] V. Rothmund: Zeitschr. f. physik. Chem., *63*, 54 (1908).

HARDY[13] declared colloid systems to be in essence mixtures of two mutually soluble substances, though he afterwards gave up this view in favor of his better known electrical theories. In 1905, D. KONOWALOW[14] declared mutually soluble systems at their critical temperature to be "colloids"; but their clear and sharp definition as "emulsoids" belongs to WOLFGANG OSTWALD.[15]

What are the physico-chemical differences that may be discovered in any system consisting of a mixture of *a* with *b*, depending upon whether *a* is dissolved in *b* or *b* is dissolved in *a*? Obviously these inverse types of solution are the analogues of the zones *A* and *Z* of the diagrams of Fig. 2. The next pages show that large qualitative and quantitative differences may be discovered between these two types of solution. Later, proof is brought that similarly large differences may be demonstrated in lyophilic colloid systems whenever these change from liquid systems to gels (when, for example, a solution of soap in water at a high temperature changes to one of water in soap as the mixture cools and sets into a gel). This is evidence, obviously, that inversion in type of solution from *a* in *b* in the former instance to *b* in *a* in the latter, actually occurs.

We shall, to this end, study first the electrical properties of two typical mutually soluble systems, namely, phenol/water and quinolin/water.

A. The System Phenol/Water

I

The two solutions which may be prepared from phenol and water, namely, phenol-dissolved-in-water and water-dissolved-in-phenol, are our analogues respectively of the zones *A* and *Z* of Fig. 2. The following paragraphs concern themselves primarily with the electrical resistances registered by these two phases. We are interested chiefly in the phase water-dissolved-in-phenol because this has received least study by the physical chemist, his interest having been principally devoted to the "dilute solution"

[14] D. KONOWALOW: Drude's Ann., *10*, 378 (1905).

[13] W. B. HARDY: Journ. Physiol., *24*, 158 (1899); Zeitschr. f. physik. Chem., *33*, 326 (1900).

[15] WO. OSTWALD: Koll.-Zeitschr., *1*, 335 (1907); Welt der vernachlässigten Dimensionen, 7.–8. Aufl. Dresden (1922); Koll.-Zeitschr., *32*, 3 (1923).

represented by a solution of phenol in water. Yet it is the inverse type of solution which, to our minds, gives the characteristic properties to the lyophilic colloid.

Our standard phenol/water systems were prepared by measuring 50 cc. of phenol, liquefied at 50° C., into 100 cc. cylinders and adding 50 cc. of water or the various solutions described in the experiments. After thorough mixing, the cylinders were set aside for 18 hours in a thermostat.

What happens when water only is added is illustrated in the cylinder marked 1 in Fig. 3. It will be observed that two solutions are formed, a lower one of phenol containing water (and usually referred to in the succeeding pages as the hydrated phenol phase) and an upper one of water containing phenol (and usually referred to as the phenolated water phase). After mutual solution has taken place, the two phases are unequal in volume. At 22° C., the phenol phase has a volume of 64 cc., the water phase one of 33 cc. That the sum of the two should not be 100 cc. is explained in part through the contraction of the phenol upon being cooled, in part through the contraction incident to the mutual solution.

Our main interest in this section is in the behavior of the hydrated phenol phase. It should be noted that as water dissolves in the pure phenol, its volume increases. In other words, the phenol "swells" some 28 to 30 percent. How this degree of swelling changes under various circumstances and how the degree of resistance of the two phases to the passage of an electric current through them changes are our first main themes of experimental inquiry.

The electrical resistance of the two phases was measured in the customary fashion with a pair of fixed, platinized platinum electrodes of the dip type by the ordinary Wheatstone bridge arrangement, and a telephone. The same electrodes, having the constant .0793, were used in all the experiments, they being repeatedly checked against a 1/50 normal potassium chlorid solution, to show that they had suffered no change.

Since the same electrodes were used throughout, the resistance values are given as observed without calculation into the terms of specific resistance.

The phenol used was specially purified for us by A. B. DAVIS, by being redistilled in glass in a vacuum (18 mm. Hg.) and at a temperature of 112° C. from the highest quality crystallized phenol which the market afforded. It is only such purified phenol which will exhibit the high initial resistance recorded in the following paragraphs. Our phenol when liquefied at a low temperature and then permitted to crystallize about the electrodes at 22° C. showed a resistance of more than 210,000 ohms. The purest phenol of the open market showed, under similar circumstances, a resistance of only 2,000 ohms. Such difference is dependent upon the presence of water, neutral salt, dissolved glass and atmospheric gases in the commercial preparation.

The water employed in our experiments was distilled from a silver still. Freshly obtained it had a resistance of 100,000 ohms. The nature of our experiments was such, however, that we could not protect our ultimate mixtures from air contamination or the effects of our glass containers. Control experiments showed that these circumstances might cut the electrical resistance of our distilled water down to 25,000 ohms.

Our findings regarding the electrical resistance of the two phases of a phenol/water system may be summarized in the following categorical statements.

1. *The electrical resistance of pure phenol is reduced progressively by every increment of water added to it up to its saturation point.* This is shown in Fig. 4 and Table I, which contains the experimental data. As the figure and the table show, phenol saturated with water keeps, under the conditions of our experiment (contamination with air and glass), a resistance of more than 20,000 ohms.

We wish now to discover the effects of various electrolytes and non-electrolytes upon this resistance.

2. *When alkali or acid is added to phenol/water, the electrical resistance of the hydrated phenol phase falls progressively with every increase in their concentration in the system.* This is illustrated in the two upper curves of Fig. 5 and Table II. Under otherwise similar experimental conditions, alkali reduces the electrical resistance more than acid. From the enormous initial resistance (more than 20,000 ohms) of the pure hydrated phenol, the fall is so great that the ultimate values attained are

TABLE I.—*Effect of increasing increments of water upon the electrical resistance of phenol. Temperature = 21° C.*

	Composition of the system	Volume of the phenol phase	Resistance in ohms
		cc.	
(1)	50 cc phenol .. .	47	210 000
(2)	50 " " + 2.5 cc H_2O	48	113 850
(3)	50 " " + 5 " "	53	50 100
(4)	50 " " + 7.5 " " .	55.5	33 712
(5)	50 " " + 10 " "	57.5	27 886
(6)	50 " " + 15 " "	62	23 321
(7)	50 " " + 25 " "	65	21 037
(8)	50 " " + 50 " " .	65	21 037

TABLE II.—*Effect of acid and of alkali upon the electrical resistance of phenol/water systems. Temperature = 22.5° C.*

	Composition of the system	Phase	Volume	Resistance in ohms
			cc.	
(1)	50 cc phenol + 50 cc H_2O	phenol	65	21 037
		water		351.81
(2)	50 " " + 50 " 1/50 n HCl . .	phenol	65	1 286
		water		9.04
(3)	50 " " + 50 " 2/50 n " .	phenol	64.5	633
		water		4.74
(4)	50 " " + 50 " 3/50 n "	phenol	64	439
		water		3.29
(5)	50 " " + 50 " 4/50 n " . .	phenol	64	346
		water		2.57
(6)	50 " " + 50 " 5/50 n "	phenol	63.5	279
		water		2.07
(7)	50 " " + 50 " 1/50 n NaOH .	phenol	66.5	570
		water		99.25
(8)	50 " " + 50 " 2/50 n "	phenol	67.5	271
		water		55.26
(9)	50 " " + 50 " 4/50 n " .	phenol	68	127
		water		30.64
(10)	50 " " + 50 " 6/50 n " ..	phenol	70.5	79
		water		22.46
(11)	50 " " + 50 " 8/50 n "	phenol	73	57
		water		18.30
(12)	50 " " + 50 " 10/50 n "	phenol	79	41
		water		15.78

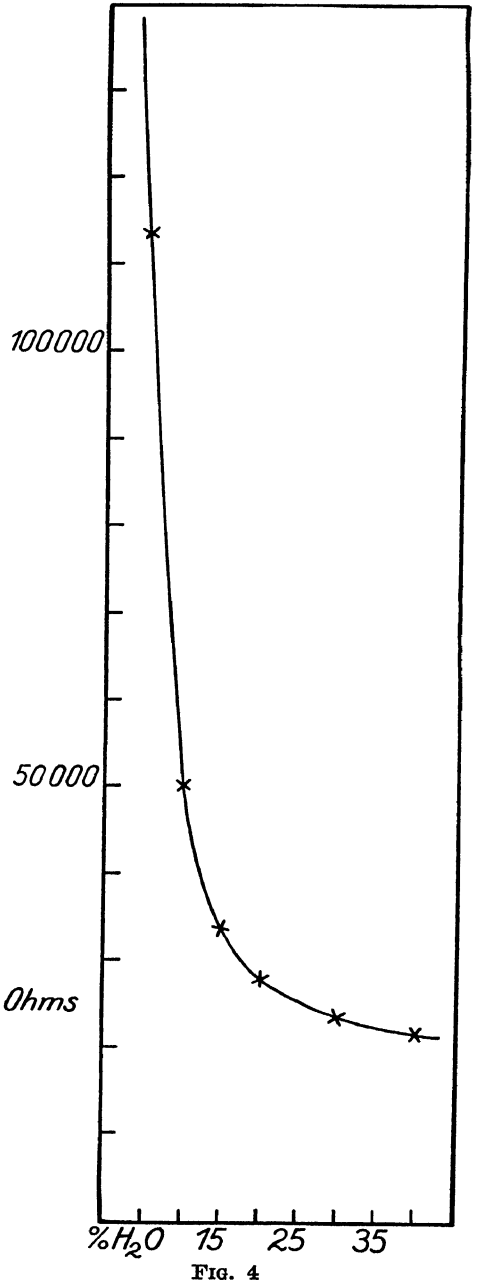
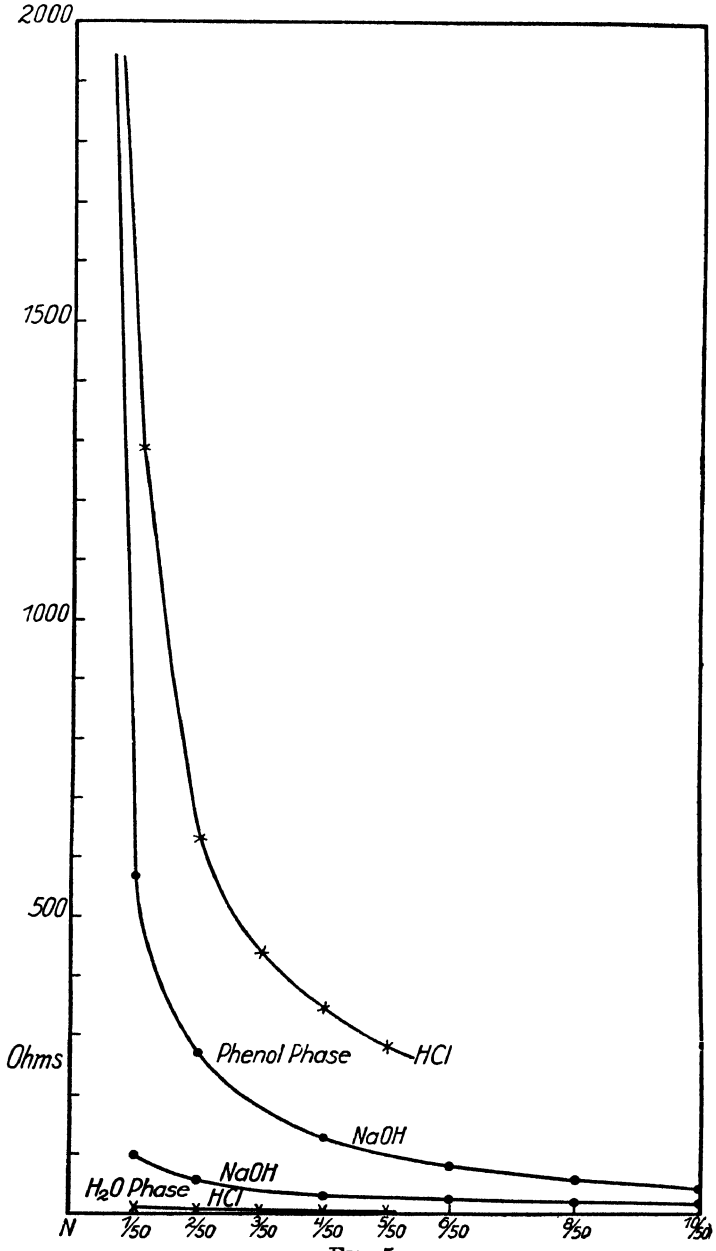


FIG. 4


2000
1500
1000
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Ohms
Phenol Phase
HCl
NaOH
NaOH
H_2O Phase
HCl
N
1/50
2/50
3/50
4/50
5/50
6/50
8/50
10/50

FIG. 5

measurable in hundreds. The two lower curves of Fig. 5 illustrate graphically the resistance of the water phases in equilibrium with the phenol phases just described.

While both acid and alkali reduce the resistance of hydrated phenol, only the latter influences markedly its volume. While acid seems to decrease it slightly, *alkali leads to a progressive increase in the volume of the phenol phase.*[16] The effect is shown in Fig. 3. In common parlance, the phenol "swells" under the influence of the alkali.

3. *When employed at the same normality, different alkalies are unequally effective in reducing the electrical resistance of hydrated phenol.* This is shown in Fig. 6 and Table III. The

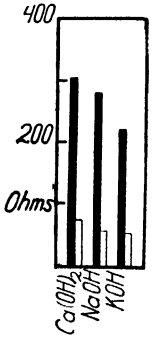


FIG. 6

TABLE III.—*Effect of different equinormal alkalies upon the electrical resistance of phenol/water systems. Temperature = 22.5° C.*

	Composition of the system	Phase	Resistance in ohms
(1)	50 cc phenol + 50 cc 2/50 n $Ca(OH)_2$ . .	phenol	303
		water	72.73
(2)	50 " " + 50 " 2/50 n NaOH	phenol	280
		water	55.71
(3)	50 " " + 50 " 2/50 n KOH	phenol	220
		water	46.22

[16] No doubt a new compound of phenol with the alkali is produced of a higher hydration capacity than the pure phenol. See the analogous behavior of protein and protoplasm on pages 138 and 216.

black columns indicate the electrical resistances of the phenol phases, the white, of the water phases. As is readily apparent, the resistance of the hydrated phenol is reduced less by calcium hydroxid than by sodium hydroxid and less by this alkali than by potassium hydroxid.

4. Fig. 7 and Tables IV and V show the effect of adding a

TABLE IV.—*Effect of different concentrations of NaCl upon the electrical resistance of phenol/water systems. Temperature = 20.5° C.*

	Composition of the system	Phase	Volume	Resistance in ohms
			cc.	
(1)	50 cc phenol + 50 cc H_2O	phenol	65	76 186
		water		2 302
(2)	50 " " + 50 cc 1/8 m NaCl	phenol	64	541
		water		5.82
(3)	50 " " + 50 " 1/4 m "	phenol	63	362
		water		3.38
(4)	50 " " + 50 " 1/2 m "	phenol	61	275
		water		1.90
(5)	50 " " + 50 " 3/4 m "	phenol	61	252
		water		1.62
(6)	50 " " + 50 " 1/1 m "	phenol	60	241
		water		1.11
(7)	50 " " + 50 " 3/2 m "	phenol	59	255
		water		0.78
(8)	50 " " + 50 " 2/1 m "	phenol	57.5	274
		water		0.63
(9)	50 " " + 50 " 3/1 m "	phenol	54.5	326
		water		0.52
(10)	50 " " + 50 " 4/1 m "	phenol	53.5	400
		water		0.48
(11)	50 " " + 50 " 5/1 m "	phenol	54.5	467
		water		0.40

neutral salt (sodium chlorid or calcium chlorid) to a phenol/water system. *The addition of such salts lowers the electrical resistance of the phenol phase.* But the nature of the salt employed and its concentration make a difference. At the same *normality,* sodium chlorid reduces the resistance more than calcium chlorid (the entire NaCl curve lies below the $CaCl_2$ curve) while the greatest reduction in resistance of the phenol phase is discovered when the salts are present in a medium concentration.

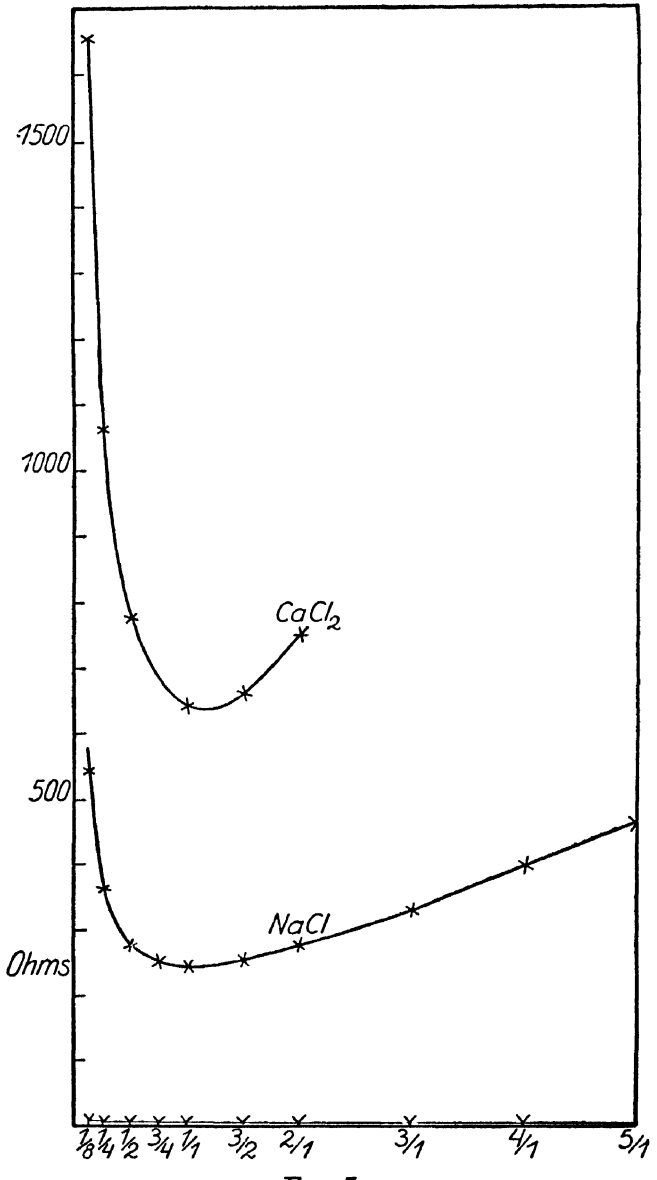


FIG. 7

TABLE V.—*Effect of different concentrations of $CaCl_2$ upon the electrical resistance of phenol/water systems. Temperature = 22° C.*

	Composition of the system	Phase	Volume	Resistance in ohms
			cc.	
(1)	50 cc phenol + 50 cc H_2O	phenol	65	27 886
		water		466
(2)	50 " " + 50 cc 1/16 m $CaCl_2$	phenol	62.5	1 655
		water		7.09
(3)	50 " " + 50 " 1/8 m "	phenol	62	1 062
		water		3.92
(4)	50 " " + 50 " 1/4 m "	phenol	60.5	776
		water		2.26
(5)	50 " " + 50 " 1/2 m "	phenol	60	642
		water		1.29
(6)	50 " " + 50 " 3/4 m "	phenol	58.5	663
		water		0.96
(7)	50 " " + 50 " 1/1 m "	phenol	56.5	750
		water		0.81

The volume of the phenol phase, on the other hand, diminishes progressively with every increase in the concentration of either of the added salts.

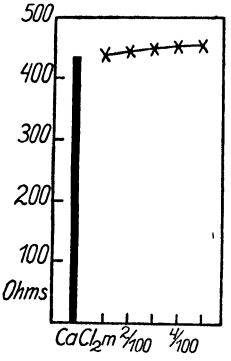


FIG. 8

5. While consideration of the preceding paragraph would by itself indicate that the substitution of calcium chlorid for sodium chlorid in a phenol/water system would be followed by an increase in electrical resistance, this fact is demonstrated directly in Fig. 8 and Table VI. The black column shows the resistance

TABLE VI.—*Antagonism between $CaCl_2$ and NaCl and their effect upon the electrical resistance of phenol/water systems. Temperature = 18.5° C.*

	Composition of the system	Phase	Volume	Resistance in ohms
			cc.	
(1)	50 cc phenol + 50 cc H_2O	phenol	65	100 100
		water		3 041
(2)	50 " " + 50 cc 1/4 m NaCl	phenol	64	435
		water		3.55
(3)	50 " " + 49 " 1/4 m NaCl + 1 cc 1/8 m $CaCl_2$	phenol	63	439
		water		3.55
(4)	50 " " + 48 " 1/4 m " + 2 " 1/8 m "	phenol	63	443
		water		3.58
(5)	50 " " + 47 " 1/4 m " + 3 " 1/8 m "	phenol	62.5	448
		water		3.56
(6)	50 " " + 46 " 1/4 m " + 4 " 1/8 m "	phenol	62.5	452
		water		3.62
(7)	50 " " + 45 " 1/4 m " + 5 " 1/8 m "	phenol	61.5	454
		water		3.62

of the phenol phase when in contact with a pure 1/4 molar sodium chlorid solution. As the sodium chlorid is replaced by an equinormal amount of calcium chlorid there is a progressive increase in electrical resistance, as the short curve shows.

6. *At the same molar concentration the decrease in the electrical resistance of hydrated phenol upon the addition of a salt varies with the nature of the acid radical* when salts with a common base are compared. This is shown in Fig. 9 and Table VII.

TABLE VII.—*Effects of equimolar concentrations of different potassium salts upon the electrical resistance of phenol/water systems. Temperature = 22.5° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 50 cc phenol + 50 cc H_2O	phenol	65.5	76 263
	water		1 816
(2) 50 " " + 50 cc 1/8 m KCNS	phenol	64	200
	water		6.00
(3) 50 " " + 50 " 1/8 m KNO_3	phenol	63.5	300
	water		5.74
(4) 50 " " + 50 " 1/8 m KI	phenol	64	306
	water		5.03
(5) 50 " " + 50 " 1/8 m $KClO_3$	phenol	64	326
	water		5.74
(6) 50 " " + 50 " 1/8 m KBr	phenol	64	369
	water		5.03
(7) 50 " " + 50 " 1/8 m KCl	phenol	64	389
	water		5.08
(8) 50 " " + 50 " 1/8 m $K_2C_2O_4$	phenol	63.5	782
	water		3.29
(9) 50 " " + 50 " 1/8 m $K_2C_4H_4O_6$	phenol	63.5	881
	water		3.73
(10) 50 " " + 50 " 1/8 m K_2SO_4 . .	phenol	63	1 112
	water		3.36
(11) 50 " " + 50 " 1/8 m neut. K phos. ($KH_2PO_4 + K_2HPO_4$)	phenol	64	1 087
	water		7.18

While there is a difference even between the individual members of any group, the following general statement holds. *Monovalent acid radicals reduce the electrical resistance of the phenol*

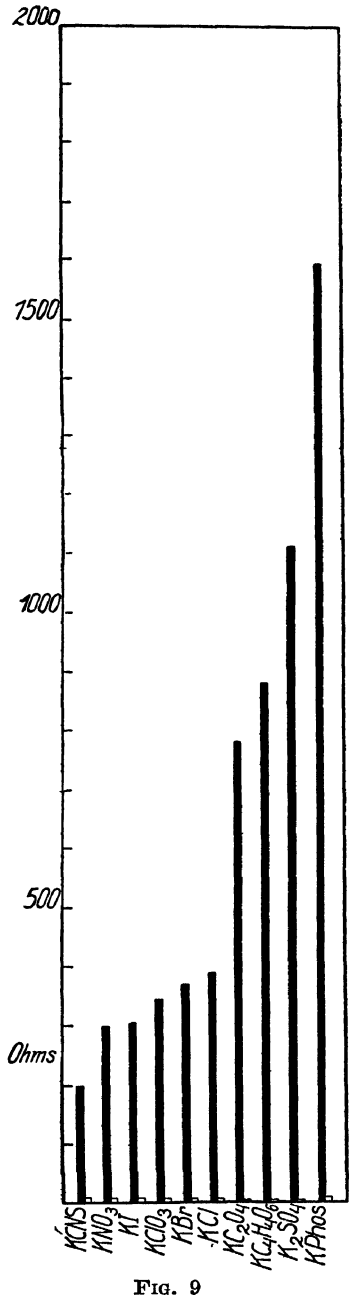

2000
1500
1000
500
Ohms
KCNS
KNO3
KI
KClO3
KBr
KCl
KC2O4
KC4H5O6
K2SO4
KPhos

FIG. 9

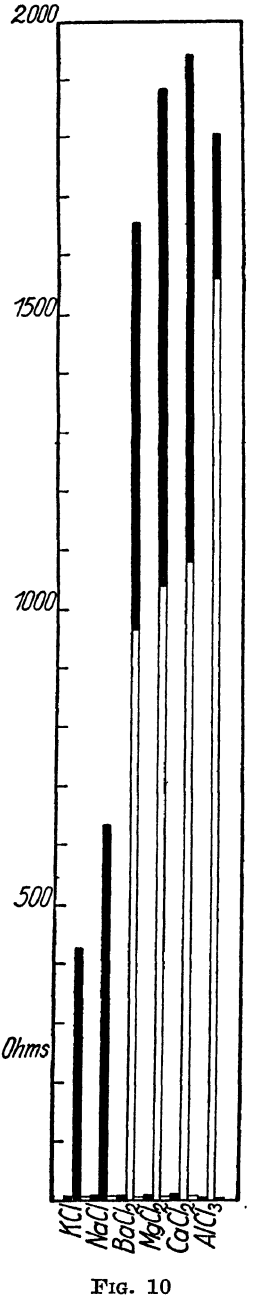

2000
1500
1000
500
Ohms
KCl
NaCl
BaCl2
MgCl2
CaCl2
AlCl3

FIG. 10

phase more than do the divalent ones and these more than the trivalent ones.

When salts with a common acid radical (chlorids) are compared, *the effects of the bases are found to be different.* Here again *divalent radicals are less effective in decreasing the resistance than monovalent ones and the trivalent aluminium less than the divalent alkaline earths.* The matter is illustrated in Fig. 10 based upon the experimental findings detailed in Tables VIII and IX. The first two black columns and the succeeding

TABLE VIII.—*Effect of equimolar concentrations of different chlorids upon the electrical resistance of phenol/water systems. Temperature = 22.5° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 50 cc phenol + 50 cc H_2O .	phenol	65.5	63 433
	water		1 286
(2) 50 " " + 50 cc 1/8 m KCl .	phenol	62.5	377
	water		5.10
(3) 50 " " + 50 " 1/8 m NaCl . .	phenol	63	594
	water		6.00
(4) 50 " " + 50 " 1/8 m $BaCl_2$.	phenol	63	961
	water		3.29
(5) 50 " " + 59 " 1/8 m $MgCl_2$ . .	phenol	62.5	1 038
	water		3.69
(6) 50 " " + 50 " 1/8 m $CaCl_2$ . .	phenol	62	1 077
	water		3.88
(7) 50 " " + 50 " 1/8 m $AlCl_3$.	phenol	62.5	1 557
	water		2.95

tall white columns show the differences when the salts are compared in *equimolar* concentrations; the black extensions, when compared in *equinormal* concentrations.

The effects of the different salts in the concentrations employed upon the volume of the phenol phase are too slight to be noteworthy.

7. The effect of adding anhydrous ethyl alcohol to phenol/water is shown in Fig. 11 and Table X. *The addition of increasing amounts of ethyl alcohol at first lowers the electrical resistance of hydrated phenol from more than 20,000 ohms to 5,000 ohms and then increases it to nearly twice the original value.*

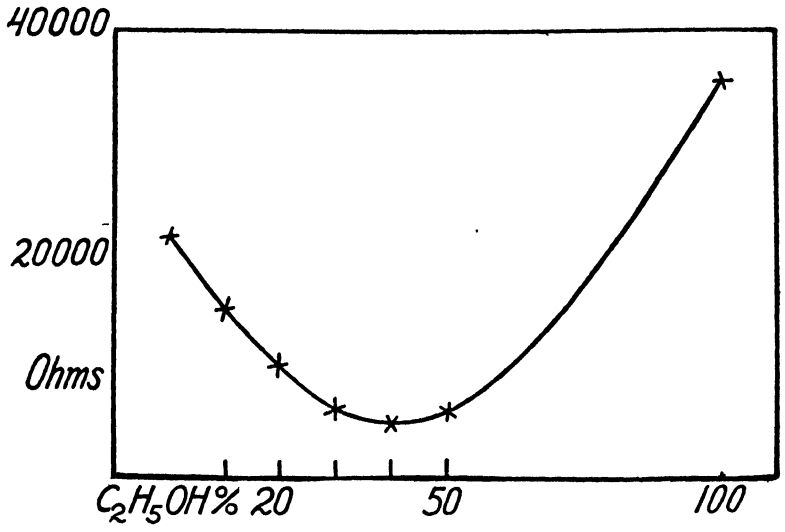


FIG. 11

While ethyl alcohol at proper concentration lowers the electrical resistance of hydrated phenol, it is less effective in this regard than any of the ordinary electrolytes.

TABLE IX.—*Effect of equinormal concentrations of different chlorids upon the electrical resistance of phenol/water systems. Temperature = 19.75° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 50 cc phenol + 50 cc H_2O	phenol	64	100 100
	water		3 126
(2) 50 " " + 50 cc 1/8 n KCl	phenol	62	422
	water		5.38
(3) 50 " " + 50 " 1/8 n NaCl .	phenol	61.5	633
	water		6.39
(4) 50 " " + 50 " 1/8 n $BaCl_2$ . .	phenol	63.5	1 655
	water		6.26
(5) 50 " " + 50 " 1/8 n $MgCl_2$.	phenol	62.5	1 880
	water		6.94
(6) 50 " " + 50 " 1/8 n $CaCl_2$ . . .	phenol	63	1 939
	water		7.54
(7) 50 " " + 50 " 1/8 n $AlCl_3$.	phenal	62	1 814
	water		3.12

TABLE X.—*Effect of increasing increments of ethyl alcohol upon the electrical resistance of phenol/water systems. Temperature = 23° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 50 cc phenol + 50 cc H_2O	phenol	64	21 476
	water		324
(2) 50 " " + 5 cc abs. ethyl alcohol + 45 cc H_2O . .	phenol	68.5	15 065
	water		305
(3) 50 " " + 10 " " " " + 40 " " .	phenol	76.5	10 110
	water		275
(4) 50 " " + 15 " " " " + 35 " " .	phenol	86.5	6 163
	water		525
(5) 50 " " + 20 " " " " + 30 " " . . .	phenol	single phenol phase only	4 875
(6) 50 " " + 25 " " " " + 25 " " . .	phenol		5 727
(7) 50 " " + 50 " " " "	phenol		35 678

TABLE XI.—*Effect of equal volumes of different monatomic alcohols upon the electrical resistance of phenol/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 50 cc phenol + 50 cc H_2O	phenol	63	22 027
	water		350
(2) 50 " " + 10 cc methyl alcohol + 40 cc H_2O	phenol	81.5	5 204
	water		369
(3) 50 " " + 10 " ethyl alcohol + 40 " "	phenol	74.5	12 123
	water		307
(4) 50 " " + 10 " propyl alcohol + 40 " "	phenol	69.5	27 679
	water		272
(5) 50 " " + 10 " (iso) butyl alcohol + 40 " "	phenol	67.5	45 000
	water		261
(6) 50 " " + 10 " (iso) amyl alcohol + 40 " "	phenol	66.5	71 923
	water		250

The volume changes which the phenol phase shows under the conditions of the experiment just described are illustrated in Fig. 12 which is a photograph of the first five tubes of the series detailed in the table. When the mixture marked 5 is reached, the phenol phase looks like an ordinary aqueous solution but that it is not such is readily proved by adding more water. The added water continues to form a separate phase above the already described mixture.

8. Fig. 13 and Table XI show that *of a series of monatomic alcohols, it is only the lower members which bring about a decrease in the electrical resistance of hydrated phenol.* The first black column shows the electrical resistance of the hydrated phenol control. Only upon the addition of methyl or ethyl alcohols is the height of this column reduced. Propyl, butyl and amyl alcohols increase the resistance. In these experiments equal volumes of the different alcohols were used. When equimolar amounts are employed, the described electrical differences are further exaggerated.

The addition of any of these alcohols leads to increased "swelling" of the phenol phase. It is greatest, however, with the lowermost members of the alcohol series.

II

We have no desire to enter at this time upon any detailed discussion of the nature of the causes for the electrical changes which are observed in the experiments that have been described. This would involve us in a debate regarding the fundamental nature of conductivity in solutions, a thing we wish to avoid. The following facts, however, deserve emphasis.

It is clear that phenol and water yield at least two types of true solution. The broadly accepted view of the physical chemists, that their molecular dispersions of one material in a second are always to be thought of as systems of one type only, needs, therefore, to be revised. Since the two phases will not mix excepting to form a frank emulsion, it follows as a matter of necessity that a solution of phenol in water, for example, has a structure definitely different from one of water in phenol. The solution of phenol in water is the one upon which physical chemists have bestowed chief study. It is the water in phenol type

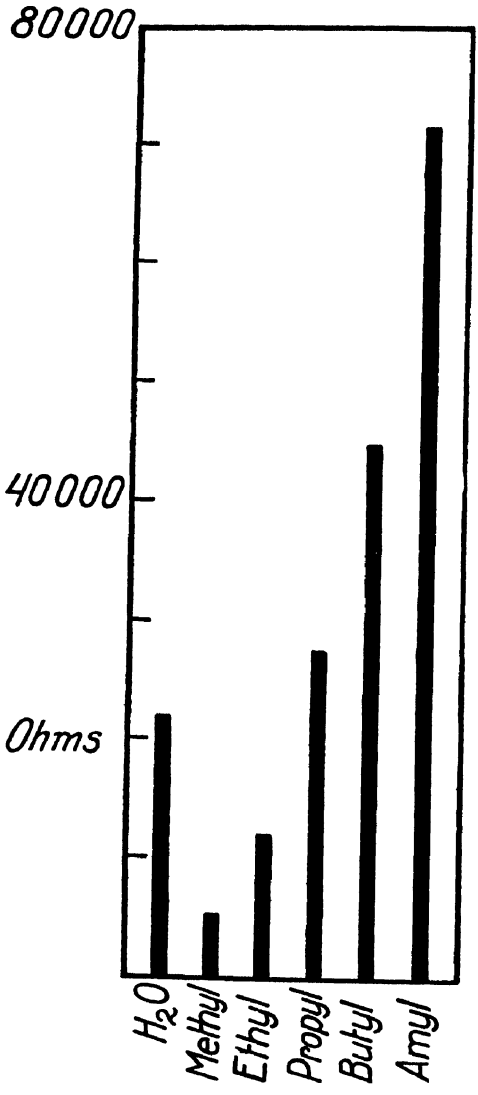


FIG. 13

of solution, however, which bears the closer analogy to living matter and it is, therefore, the physical chemistry of this system which we may expect to find more directly applicable to protoplasm.[16a]

It will be found similarly applicable, of course, to all systems of the lyophilic colloid type. But what we venture to suggest even here is that the physical chemistry of this inverse type of solution will serve to explain much of the "exceptional" behavior which the "true" solutions show when "concentrated," for example. As such concentration takes place, materials having the structure solvent-dissolved-in-dissolved-substance must appear in increasing amount and must in this proportion modify the linear laws characteristic of the classical "dilute" solutions.[17]

The findings described in the preceding paragraphs indicate also that several factors need to be considered when any interpretation of the electrical changes observed is attempted. When acid or alkali is added to hydrated phenol, there is a decrease in the electrical resistance just as when acid or alkali is added to water. This observation might be interpreted as the direct consequence of the solution of an electrolyte in the hydrated phenol with secondary electrical dissociation of the dissolved materials as in the case of pure water. Something more, however, happens, for while the addition of acid does not markedly influence the volume of the hydrated phenol phase, the addition of alkali enormously increases its water-holding capacity.

In the case of the neutral salts, reduction in the electrical resistance might again be conceived of as due to solution of the salts in the hydrated phenol and their ionization. Their less ready solubility and lower degree of ionization in this medium might then be used to explain the lesser effects of trivalent salts as compared with divalent ones, and these as compared with monovalent ones. This simple idea is also disturbed if the hydrated phenol is investigated when in equilibrium with an aqueous solution of the electrolyte. With ascending concentration of the latter, the water-holding power of the hydrated phenol is increasingly diminished. Obviously, final answer to

[16a] See the argument under this head on p. 221.

[17] See the observations on sulphuric acid, p. 99.

the qualitative and quantitative nature of the various changes involved will require analyses directed to the distribution of water, phenol and electrolyte in the two phases and their volumes.

The effects of the alcohols suggest further interesting problems. In spite of their classification as non-electrolytes, the lower alcohols bring about a decrease in electrical resistance when added to water/phenol systems. With progressive additions, however, the resistance of the hydrated phenol rises and this is accomplished in spite of a progressive increase in the volume of the hydrated phenol. To understand the latter fact, in such apparent contradiction to the behavior of the salts, it will be necessary, we think, to have recourse to an opinion expressed before, namely, that even the true solution represents more than a molecular dispersion of one material in a second. There is, in addition, union with solvent.[18] When a salt solution covers the hydrated phenol phase, the salt particles may unite with the water and so abstract it from the hydrated phenol and thus diminish the volume of the latter. In the case of alcohol, there is possible a similar union with water, but the tendency of the alcohol to unite with the phenol, especially in the case of the higher alcohols, is even greater.

B. The System Quinolin/Water[19]

Like phenol and water, quinolin and water also yield a mutually soluble system, but the mutual solubility is not so great. At 20° a liter of water dissolves only 1 cc. of quinolin but one liter of quinolin dissolves 100 cc. of water. Quinolin was chosen for these studies as a substance more definitely basic in character to compare with the more definitely acid phenol of the preceding paragraphs.

[18] It needs constantly to be borne in mind that such hydration (or solvation in general) may also be of *at least two* kinds. The water united to a neutral salt in the ordinary salt solution, for example, must be combined with this (as witness its liquid character) in a fashion other than the water united with this same salt as (solid) water of crystallization. The same is true of the soaps when dissolved in water, and when these soaps have "dissolved" the water.

[19] MARTIN H. FISCHER: Science, *57*, 724 (1923); Kolloid-Zeitschr. *33*, 208 (1923).

Experimental procedure was identical with that already described, the same pair of dip electrodes (of the constant .0793) being used. The stock quinolin was one specially purified by A. B. DAVIS.

1. We wished to determine, first, the change in the electrical resistance of quinolin as more and more water is added to the "dry" quinolin up to its saturation point. Our pure quinolin showed by itself an electrical resistance of more than 400,000 ohms. Fig. 14 and Table XII show how upon the addition of

TABLE XII.—*Effect of increasing increments of water upon the electrical resistance of quinolin. Temperature = 24° C.*

Composition of the system	Resistance in ohms
(1) 100 cc quinolin	420 534
(2) 100 " " + 2 cc H_2O	320 100
(3) 100 " " + 4 " "	220 332
(4) 100 " " + 6 " "	142 407
(5) 100 " " + 8 " "	103 893
(6) 100 " " + 10 cc "	78 492

increasing increments of water this falls progressively until a final resistance of approximately 80,000 ohms is registered when saturation is complete at 24°.

2. We wished now to discover how the electrical resistance of such hydrated quinolin would vary upon the addition of various electrolytes and non-electrolytes. For this purpose we prepared quinolin/water systems as in our studies upon phenol/water systems. In each instance there were added to 25 cc. of quinolin 25 cc. of water or the necessary solution of an electrolyte or non-electrolyte. How the electrical resistance of hydrated quinolin is progressively reduced with every increase in the concentration of an added acid or alkali is illustrated in Fig. 15 and Table XIII.

Potassium hydroxid produces less reduction in electrical resistance than does equinormal hydrochloric acid, a behavior the opposite of that noted for hydrated phenol. Neither substance affects markedly the volume of the hydrated quinolin, only a slight diminution being evident in both instances.

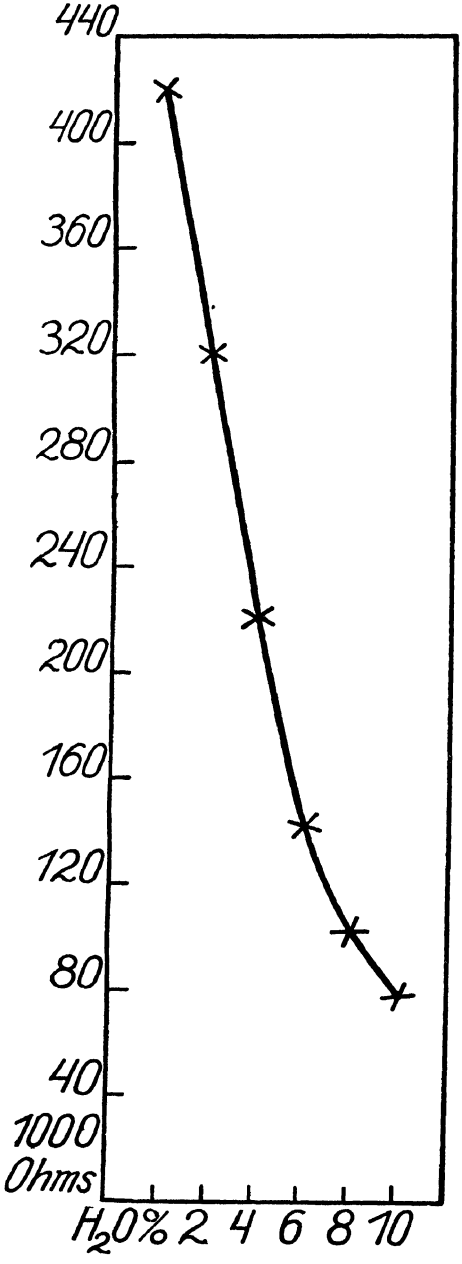


FIG. 14

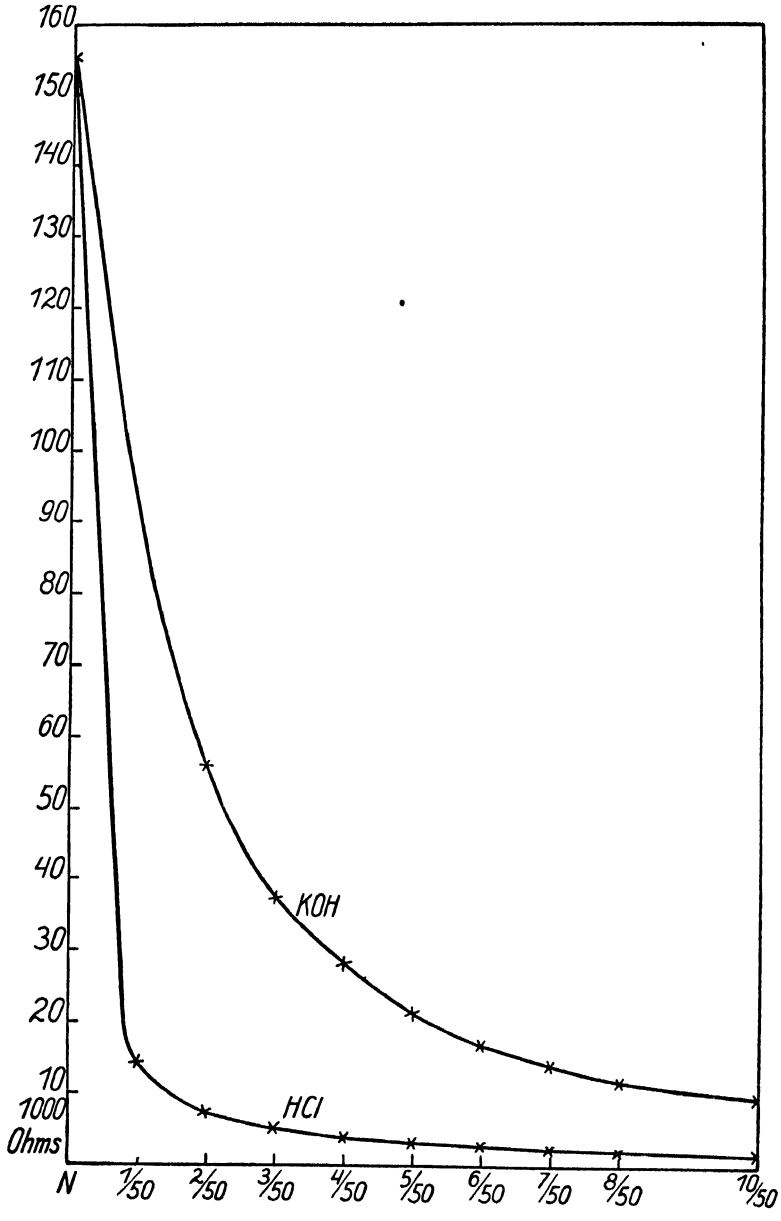

160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
1000
Ohms
KOH
HCl
N
1/50
2/50
3/50
4/50
5/50
6/50
7/50
8/50
10/50

FIG. 15

TABLE XIII.—*Effect of acid and of alkali upon the electrical resistance of quinolin/water systems. Temperature = 23° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O	quinolin	28	155 100*
	water		1 297.35
(2) 25 " " + 25 cc 1/50 n HCl . .	quinolin	27	14 376
	water		45.10
(3) 25 " " + 25 " 2/50 n " . . .	quinolin	27	7 317
	water		24.51
(4) 25 " " + 25 " 3/50 n " . . .	quinolin	27	4 942
	water		17.14
(5) 25 " " + 25 " 4/50 n "	quinolin	26.5	3 478
	water		13.47
(6) 25 " " + 25 " 5/50 n " . . .	quinolin	26.5	2 990
	water		11.15
(7) 25 " " + 25 " 6/50 n " .	quinolin	26.5	2 500
	water		9.81
(8) 25 " " + 25 " 7/50 n " . .	quinolin	26.5	2 045
	water		8.66
(9) 25 " " + 25 " 8/50 n " .	quinolin	26.5	1 847
	water		7.78
(10) 25 " " + 25 " 10/50 n " . . .	quinolin	26	1 500
	water		6.72
(11) 25 cc quinolin + 25 cc H_2O	quinolin	28	155 100
	water		1 437.98
(12) 25 " " + 25 cc 1/50 n KOH .	quinolin	28	69 928
	water		46.44
(13) 25 " " + 25 " 2/50 n "	quinolin	27.5	56 100
	water		20.33
(14) 25 " " + 25 " 3/50 n " . .	quinolin	27	37 242
	water		14.64
(15) 25 " " + 25 " 4/50 n " .	quinolin	27	28 176
	water		11.15
(16) 25 " " + 25 " 5/50 n " . . .	quinolin	27	21 037
	water		9.38
(17) 25 " " + 25 " 6/50 n "	quinolin	27	16 856
	water		7.73
(18) 25 " " + 25 " 7/50 n " .	quinolin	27	13 955
	water		6.62
(19) 25 " " + 25 " 8/50 n " . .	quinolin	27	11 621
	water		6.13
(20) 25 " " + 25 " 10/50 n "	quinolin	27	9 511
	water		5.04

* See the footnote on p. 37.

TABLE XIV.—*Effect of different equinormal acids upon the electrical resistance of quinolin/water systems. Temperature = 20.5° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc 1/50 n HCl .	quinolin	27	14 544
	water		51.95
(2) 25 " " + 25 " 1/50 n lactic acid	quinolin	27	33 905
	water		76.95
(3) 25 " " + 25 " 1/50 n acetic acid	quinolin	27	40 358
	water		73.96
(4) 25 " " + 25 " 1/50 n oxalic acid	quinolin	27	81 766
	water		51.95
(5) 25 " " + 25 " 1/50 n H_2SO_4 .	quinolin	27	114 850
	water		50.49

3. At the same normality, different acids bring about an unequal lowering in the electrical resistance of hydrated quinolin as evident in Fig. 16 and Table XIV. The same is true of alkalies as shown in Fig. 17 and Table XV. In the case of the

TABLE XV.—*Effect of different equinormal alkalies upon the electrical resistance of quinolin/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O . . .	quinolin	27.5	155 100
	water		1 610.96
(2) 25 " " + 25 " 1/50 n NH_4OH	quinolin	27.5	113 850
	water		164.55
(3) 25 " " + 25 " 1/50 n KOH . . .	quinolin	27.5	68 970
	water		39.47
(4) 25 " " + 25 " 1/50 n NaOH	quinolin	27.5	80 100
	water		51.51
(5) 25 " " + 25 " 1/50 n $Ca(OH)_2$	quinolin	27.5	84 385
	water		71.23

* To get complete saturation of the quinolin with water requires continuous shaking over several days. The readings in this and the subsequent tables were made after the mixtures had all been shaken several times in exactly the same way and had then been given 24 hours in which to separate. Under such circumstances saturation is *not* attained, which accounts for the higher resistance recorded here and in the subsequent tables than in the main text.

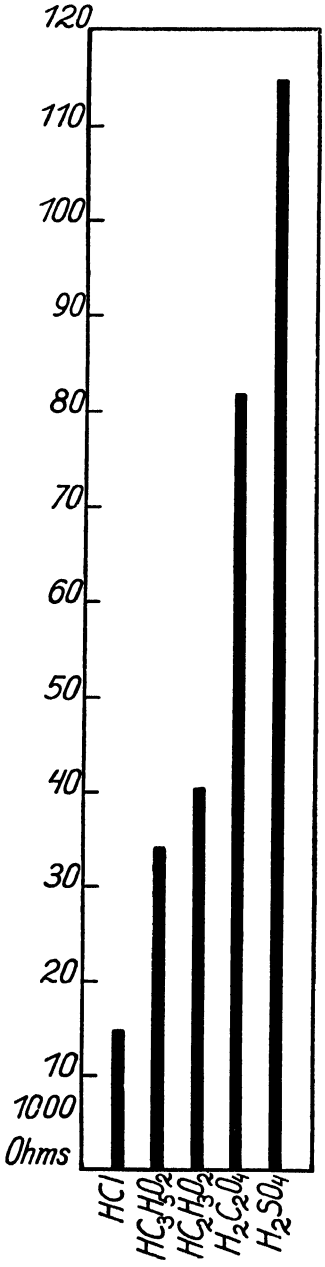

120
110
100
90
80
70
60
50
40
30
20
10
1000
Ohms
HCl
$HC_3H_5O_2$
$HC_2H_3O_2$
$H_2C_2O_4$
H_2SO_4

FIG. 16

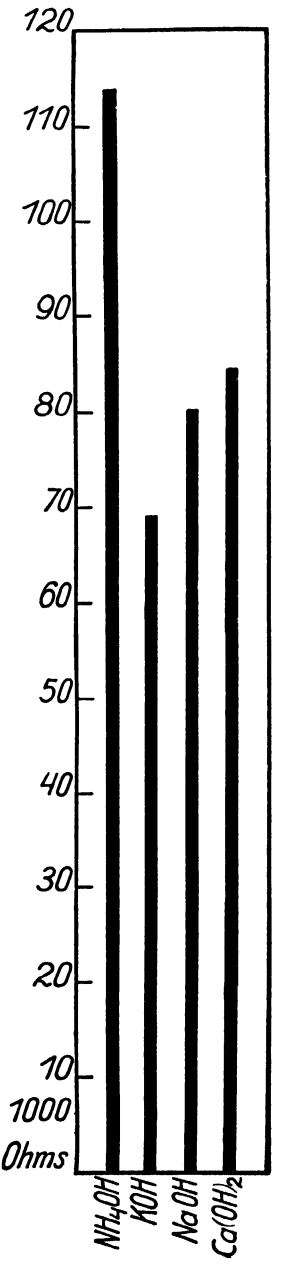

120
110
100
90
80
70
60
50
40
30
20
10
1000
Ohms
NH_4OH
KOH
NaOH
$Ca(OH)_2$

FIG. 17

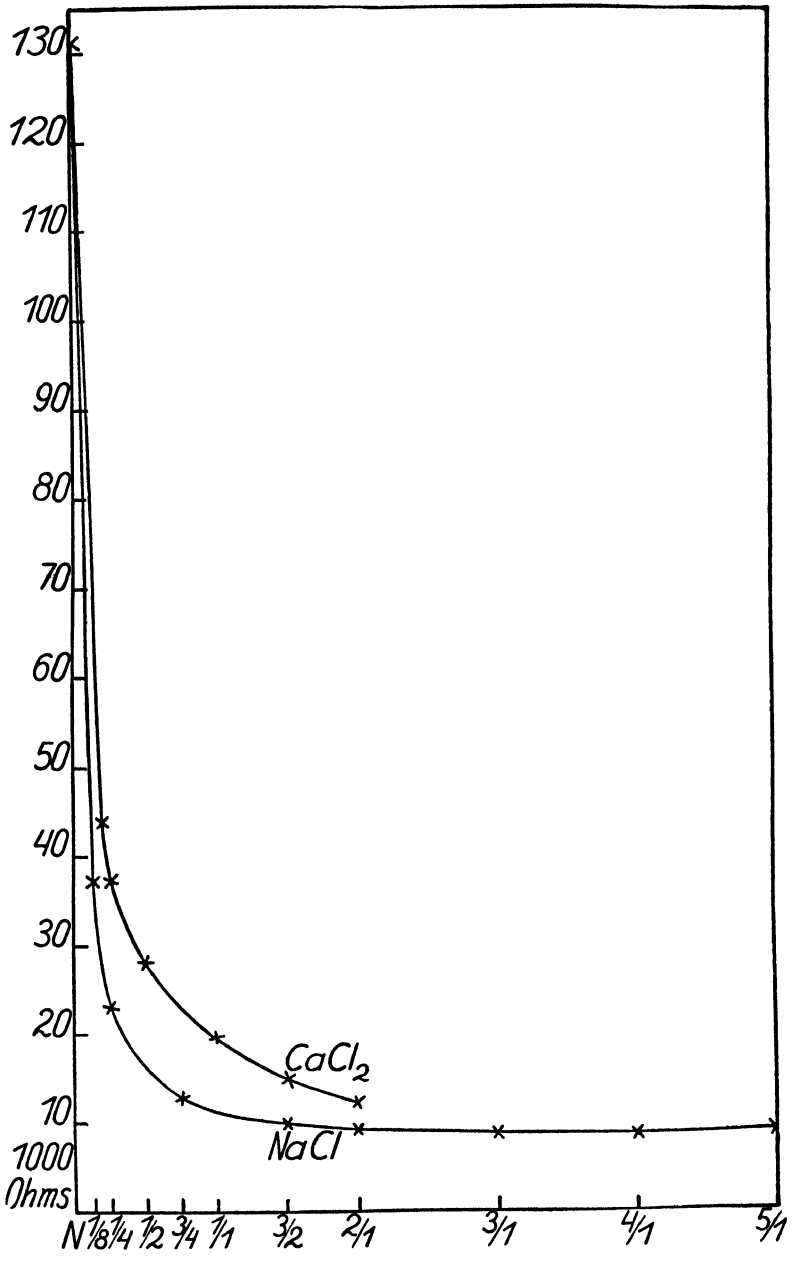

130
120
110
100
90
80
70
60
50
40
30
20
10
1000 Ohms
CaCl2
NaCl
N
1/8
1/4
1/2
3/4
1/1
3/2
2/1
3/1
4/1
5/1

FIG. 18

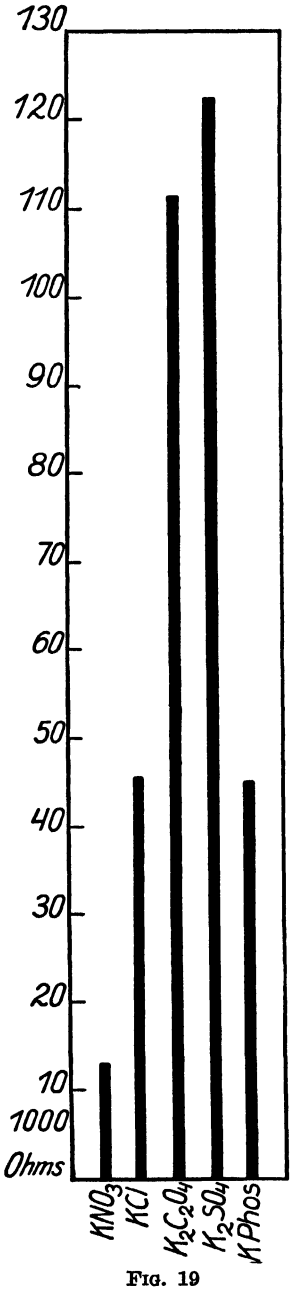


FIG. 19

acids (with a "strong" acid standing at the beginning and at the end of the list and with several "weaker" ones between) there is obviously no simple relationship between the concentration of the hydrogen ions in the aqueous solutions and the electrical resistance of hydrated quinolin. It may be stated as a general truth, however, that bivalent acids reduce the electrical resistance less than do monovalent. With the exception of the ammonium hydroxid, the same is true of the alkalies.

4. The addition of a neutral salt to a quinolin/water system reduces the resistance of the hydrated quinolin as shown in Fig. 18 and Tables XVI and XVII. At the same normality, sodium chlorid is more effective in this regard than calcium chlorid. After a low point of least resistance has been passed with progressive increase in the amount of sodium chlorid added, there follows a slight increase in the electrical resistance of the hydrated quinolin.

Both sodium chlorid and calcium chlorid affect the volume of the hydrated quinolin phase. While the amount of shrinkage is not great, it is definite and progressive with increasing concentration of the salts.

5. When the effects are compared of equimolar solutions of a series of salts with a common base but with different acid radicals, an unequal effect upon the electrical resistance of the hydrated quinolin is to be observed as shown in Fig. 19 and Table

XVIII. With the exception of the phosphate, the salts of the higher valency are less effective than those of lower valency in reducing electrical resistance, while the order in which they do this within these groups is that found above in the case of the pure acids and previously upon the system phenol/water.

TABLE XVI.—*Effect of increasing concentrations of NaCl upon the electrical resistance of quinolin/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O	quinolin	27.5	131 528
	water		1 077.28
(2) 25 " " + 25 cc 1/8 m NaCl	quinolin	27.5	37 242
	water		6.39
(3) 25 " " + 25 " 1/4 m "	quinolin	27.5	23 100
	water		3.42
(4) 25 " " + 25 " 1/2 m "	quinolin	27.5	19 217
	water		1.87
(5) 25 " " + 25 " 3/4 m "	quinolin	27.5	12 600
	water		1.36
(6) 25 " " + 25 " 1/1 m "	quinolin	27.5	11 163
	water		1.08
(7) 25 " " + 25 " 3/2 m "	quinolin	27.5	9 900
	water		0.81
(8) 25 " " + 25 " 2/1 m "	quinolin	26.5	9 138
	water		0.97
(9) 25 " " + 25 " 3/1 m "	quinolin	26	8 433
	water		0.49
(10) 25 " " + 25 " 4/1 m "	quinolin	25.5	8 433
	water		0.43
(11) 25 " " + 25 " 5/1 m "	quinolin	25.5	8 779
	water		0.40

6. The effect upon resistance of adding anhydrous ethyl alcohol to quinolin/water is shown in Fig. 20 and Table XIX. Progressive increase in the concentration of the alcohol in the system leads at first to a lowering of the electrical resistance of the hydrated quinolin to be followed later by an increase. While the changes in resistance describe a curve possessed of a minimum, the changes in the volume of the quinolin phase are progressive. Every increment of alcohol added mirrors itself

in an increased "swelling" of the quinolin phase, the amount of which is indicated in Table XIX.

TABLE XVII.—*Effect of increasing concentrations of $CaCl_2$ upon the electrical resistance of quinolin/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O . .	quinolin	27.5	131 528
	water		1 066.11
(2) 25 " " + 25 cc 1/16 m $CaCl_2$	quinolin	27.5	43 613
	water		6.58
(3) 25 " " + 25 " 1/8 m "	quinolin	27.5	37 242
	water		4.24
(4) 25 " " + 25 " 1/4 m " .	quinolin	27	28 176
	water		2.37
(5) 25 " " + 25 " 1/2 m "	quinolin	27	19 652
	water		1.36
(6) 25 " " + 25 " 3/4 m " . .	quinolin	27	14 850
	water		1.01
(7) 25 " " + 25 " 1/1 m " .	quinolin	26.5	11 390
	water		0.81

TABLE XVIII.—*Effect of equimolar concentrations of different potassium salts upon the electrical resistance of quinolin/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O	quinolin	27.5	155 100
	water		1 610.96
(2) 25 " " + 25 cc 1/8 m KNO_3	quinolin	27.5	12 858
	water		5.62
(3) 25 " " + 25 " 1/8 m KCl .	quinolin	27.5	45 100
	water		5.26
(4) 25 " " + 25 " 1/8 m K_2 oxalate	quinolin	27.5	110 831
	water		3.42
(5) 25 " " + 25 " 1/8 m K_2SO_4 . .	quinolin	27	122 100
	water		3.47
(6) 25 " " + 25 " 1/8 m neut. K phos. .	quinolin	26	44 495
	water		6.12

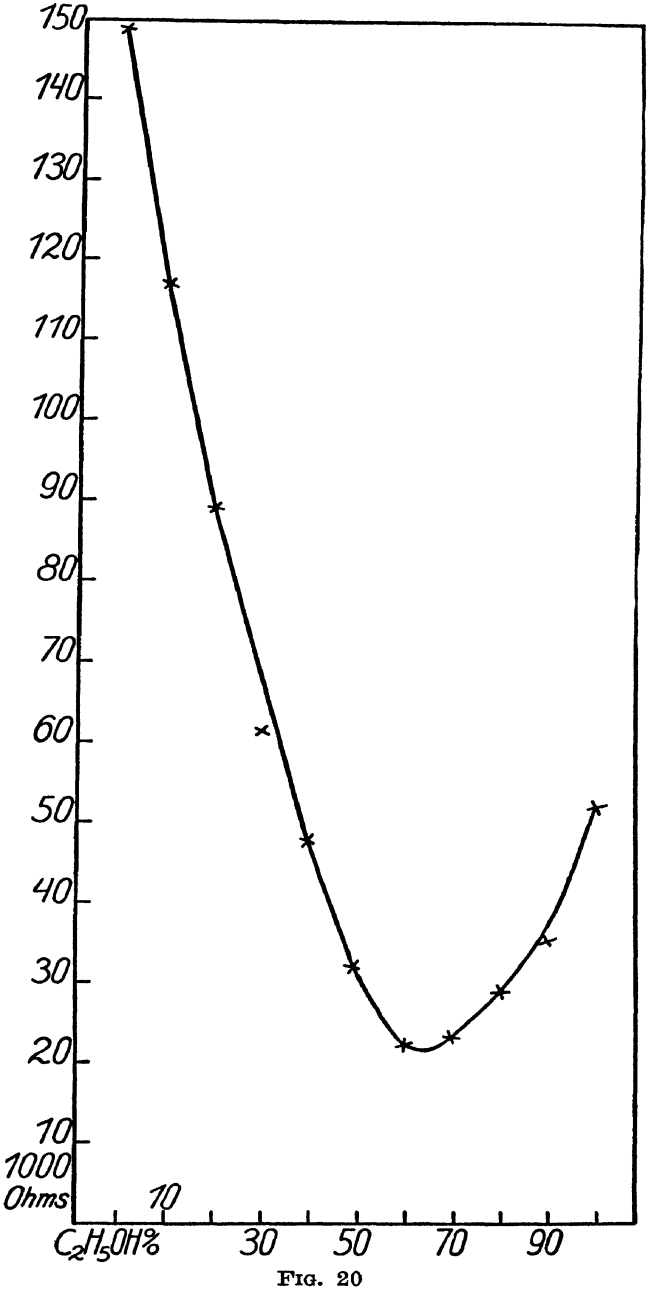

150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
1000
Ohms
10
C_2H_5OH%
30
50
70
90

FIG. 20

TABLE XIX.—*Effect of increasing increments of ethyl alcohol upon the electrical resistance of quinolin/water systems. Temperature = 22° C.*

Composition of the system	Phase	Volume	Resistance in ohms
		cc.	
(1) 25 cc quinolin + 25 cc H_2O	quinolin	27.5	147 777
	water		1 149.10
(2) 25 " " + 2.5 cc abs. ethyl alc. + 22.5 cc H_2O ..	quinolin	28.5	117 023
	water		1 350
(3) 25 " " + 5 " " " " + 20 " " .	quinolin	30.5	89 100
	water		1 571.42
(4) 25 " " + 7.5 " " " " + 17.5 " " ..	quinolin	33	61 300
	water		1 838.77
(5) 25 " " + 10 " " " " + 15 " " ..	quinolin	36	47 658
	water		1 838.77
(6) 25 " " + 12.5 " " " " + 12.5 " " ..	quinolin	40	31 872
(7) 25 " " + 15 " " " " + 10 " " .	quinolin	47	22 035
(8) 25 " " + 17.5 " " " " + 7.5 " "	quinolin	single quinolin phase only	23 100
(9) 25 " " + 20 " " " " + 5 " " ...	quinolin		28 923
(10) 25 " " + 22.5 " " " " + 2.5 " " ..	quinolin		35 100
(11) 25 " " + 25 " " " "	quinolin		51 975

C. Phenol/Water Systems in the Critical Realm[20]

The two previous sections on mutually soluble systems have detailed the differences in the matter of electrical resistance exhibited by the pure phases phenol- or quinolin-dissolved-in-water and water-dissolved-in-phenol or -quinolin.

We wish now to describe *the changes in electrical resistance observable when a solution of phenol-in-water changes to one of water-in-phenol.* This change, as induced, for example, by allowing a hot mixture of water and phenol to cool, we hold to be comparable to that which may be observed in any of the lyophilic colloids, as soap with water, when hot mixtures of these materials are chilled. In both cases we deal with what is originally a solution of the phenol or soap in the water, followed by an emulsion of the hydrated phenol or soap in the true solution, succeeded by an emulsion of the reverse type, namely, solution dispersed in hydrate, to end with a molecular solution of the water in the phenol or soap.

We used in the following experiments the same highly purified phenol previously employed. The electrical measurements were carried out as before, with the same pair of fixed platinized platinum electrodes of the dip type (again of the constant 0.0793) a Wheatstone bridge arrangement and a telephone. The mixtures of phenol and water, of the composition given in the tables, were measured and mixed at 90° C. After being thus prepared they were permitted to cool spontaneously to room temperature, the rate of chilling being fairly constant as equal volumes of the different mixtures were always cooled in the same 150 cc. beaker. There was no stirring during the chilling process. In spite of some uncontrollable errors incident to this experimental procedure, we found the readings of the electrical resistance to be remarkably close in duplicate experiments.

The mixtures of phenol and water employed in these experiments are optically clear at the higher temperature and, for the sake of brevity, will be referred to as solutions of phenol in water.[21] With lowering of temperature these mixtures become

[20] MARTIN H. FISCHER: Kolloid-Zeitschr., *34*, 97 (1924).

[21] We are nevertheless of the opinion that they are *not* homogeneous. They are still mixtures of hydrated phenol with phenolated water (as evidenced, for example, by the fact that their resistance is greater than that

opalescent, then milky, separating finally into a lower phase of hydrated phenol and an upper one of phenolated water. Tables XX, XXI, XXII, XXIII, XXIV and the curves *AAA, BBB, CCC, DDD, EEE* based upon them and shown in Fig. 21 indi-

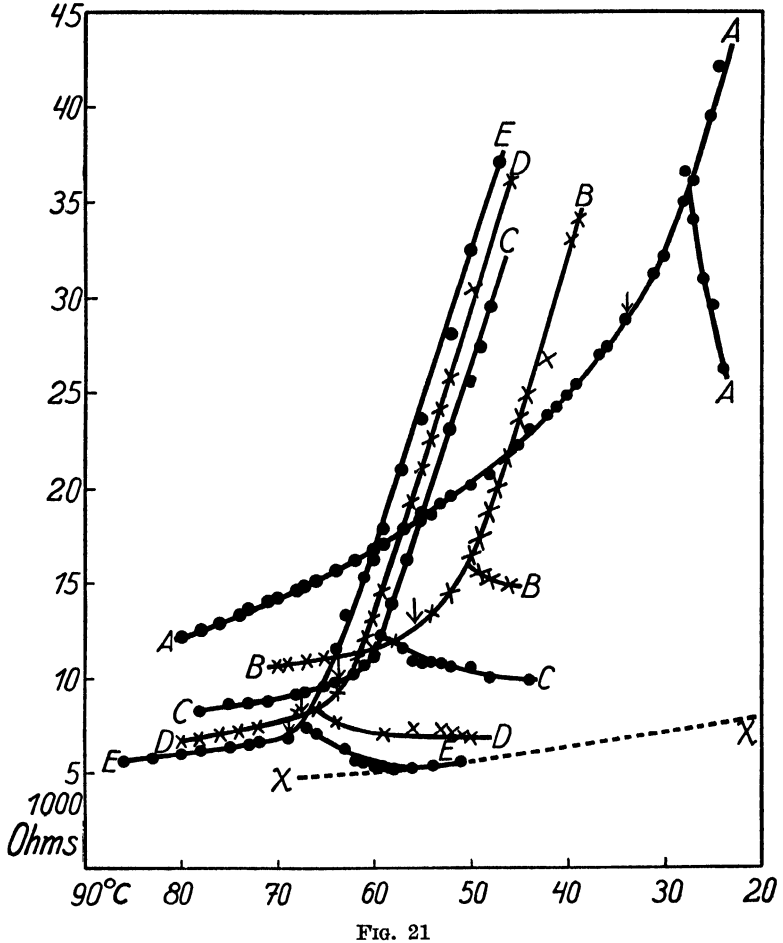


FIG. 21

cate how the electrical resistance changes as these transformations take place.

of water saturated with phenol). The beginnings of each of the curves *A, B, C, D, E* lie above the curve *XX* in Fig. 21. The importance of this idea of heterogeneity for the understanding of the "strange" behavior of various "true" solutions is commented upon later (see pp. 100 and 173).

TABLE XX.—*Changes in electrical resistance of 100 cc. phenol + 50 cc. H_2O with falling temperature*

Temperature	Bottom (ohms)	Top (ohms)
80	12 198	
78	12 600	
76	12 858	
74	13 394	
73	13 671	
71	14 070	
70	14 246	
68	14 665	
67	14 850	
66	15 163	
64	15 747	
62	16 290	
60	16 856	
59	17 149	
57	17 908	
55	18 305	
54	18 630	
53	19 217	
52	19 652	
50	20 191	
48	20 750	
46	22 035	
45	22 347	
42	23 888	
41	24 237	
40	24 836	
39	25 457	
37	27 179	
36	27 458	
*34	28 923	
31	31 350	
30	32 227	
28	35 100	36 798
27	36 186	34 100
26	37 926	31 091
25	39 600	29 700
24		26 363
22	42 205	
17	50 100	

* Distinct opalescence.

The curve AAA of Fig. 21.

If the electrical resistance of a cooling phenol/water mixture is measured near the *bottom,* the, at first, slowly mounting values show an acute *rise* which starts shortly after the system becomes opalescent. If in a duplicate run, the resistance is measured at

TABLE XXI.—*Changes in electrical resistance of 100 cc. phenol + 75 cc. H_2O with falling temperature*

Temperature	Bottom (ohms)	Top (ohms)
70	10 596	
69	10 811	
67	10 942	
65	11 119	
62	11 208	
60	11 575	
58	12 051	
*56	12 651	
54	13 504	
52	14 424	
51		15 948
50	16 500	15 747
49	17 448	15 484
48	18 795	14 850
47	20 375	
46	21 629	14 850
45	23 659	
44	24 836	
42	26 766	
40	33 143	
39	34 100	
38	34 100	

* Distinct opalescence.
Curve BBB of Fig. 21.

the *top* of the mixture, the first section of the curve rises as before, but as the opalescent region is passed, a rather sudden *fall* in electrical resistance is to be observed. The matter is to be understood, obviously, as due to the fact that in the first instances the system becomes progressively richer in the hydrated phenol phase with its low conductivity while in the latter it becomes richer in the better conducting phenolated water phase.

For purposes of comparison the curve *XX* has been drawn into Fig. 21 representing the electrical resistance of water saturated with phenol at the various temperatures.

TABLE XXII.—*Changes in electrical resistance of 100 cc. phenol + 100 cc. H_2O with falling temperature*

Temperature	Bottom (ohms)	Top (ohms)
78	8 265	
75	8 709	
73	8 779	
71	8 850	
68	9 101	
67	9 248	
65	9 665	
*64	9 860	
62	10 221	10 986
61	10 725	11 208
60	11 163	11 858
59	12 247	12 198
58	13 955	12 347
57	16 290	11 621
*56		10 942
55	18 741	10 854
54		10 854
53		10 811
52	23 100	10 682
50	25 671	10 682
49	27 458	
48	29 542	10 099
44		10 019
41		9 900
38		9 900
35		9 900

* Distinct opalescence.
Curve CCC of Fig. 21.

It needs to be added that the rather sudden changes described do not occur immediately at the critical point (the point at which a first opalescence appears, and indicated by an arrow in the curves of Fig. 21) but a little later. The reasons for this, too, are obvious. When the first optical heterogeneity manifests itself, there is not enough of the separated phase present in

either the bottom or top levels of the mixtures to change markedly the conductivity of the (external) phase which is being measured. Only somewhat later, in the region where the separating phase becomes the continuous external phase does the marked rise or fall in resistance register itself.

TABLE XXIII.—*Changes in electrical resistance of 100 cc. phenol + 150 cc. H_2O with falling temperature*

Temperature	Bottom (ohms)	Top (ohms)
80	6 738	
78	6 879	
76	7 052	
74	7 317	
72	7 468	
70	7 778	
*68	8 265	
66	8 433	
64		7 622
63	9 138	7 110
62	11 163	
61	12 198	
60	13 123	
59	14 544	7 110
57	17 987	
56	19 217	7 468 (?)
55	21 037	
54	22 559	
53	24 004	7 468 (?)
52	25 671	7 168
51		7 023
50	30 508	6 879
46	36 193	
44		6 879

* Distinct opalescence.
Curve DDD of Fig. 21.

These observations on phenol/water systems in the critical region have been detailed because in them no one doubts the existence of the two types of solution, phenol-in-water and water-in-phenol, and because the nature of the emulsions resulting when phenolated water changes to hydrated phenol is also unde-

batable. Knowing the electrical resistance of the pure phases, it is easy to understand why in the change from the system which is essentially a solution of x-in-the-solvent to one of the solvent-in-x the variations in the electrical resistance should describe the curves which have been here reproduced.

TABLE XXIV.—*Changes in electrical resistance of 100 cc. phenol + 200 cc. H_2O with falling temperature*

Temperature	Bottom (ohms)	Top (ohms)
86	5 694	
83	5 814	
80	6 067	
78	6 213	
75	6 463	
73	6 600	6 794
72	6 738	
*69	6 936	7 081
67	6 936	7 468
66	7 110	7 377
65	9 138	7 377
64	11 621	7 052
63	13 394	6 329
62		5 694
61	15 355	5 544
60	16 290	5 330
59	17 987	5 330
58		5 284
57	21 037	
56		5 284
55	23 659	
54		5 448
52	28 176	
51		5 694
50	32 589	
47	37 242	

* Distinct opalescence.
Curve EEE of Fig. 21.

The next paragraphs will show that *the same abrupt changes in electrical resistance are observable in the soaps when from a clear and apparently homogeneous solution of soap in water there are obtained an opalescent sol, a gel, and finally what is, to our minds, a (liquid or solid) solution of water in soap.*

V. The Changes in Electrical Resistance Registered by Gelling Lyophilic Colloids

The previous sections have shown that while a solution of phenol in water (or quinolin in water) is a fair conductor of electricity, a solution of water in phenol (or water in quinolin) is a much poorer one. When a mixture of water and phenol is brought from a higher temperature (from one at which it is essentially a solution of phenol in water) to a lower temperature (at which it becomes essentially a solution of water in phenol) the transition is marked by a sharp rise in electrical resistance. The following pages show that a similarly abrupt change is observable in lyophilic colloids when these are cooled, when, in other words, they are allowed to pass from what was essentially a solution of the colloid in the water to one of the water in the colloid. There are studied successively the systems soap/water, gelatin/water and casein/water.

A. The System Soap/Water[22]

The soap/water systems used in the following experiments were all prepared by adding to each other at the temperature of a boiling water bath the requisite gram equivalents of the necessary highly purified fatty acids and standard alkali solutions, the mixtures being checked for neutrality with phenolphthalein.[23] The electrical resistance was measured in the customary fashion with a fixed pair of platinized platinum electrodes of the constant 0.125. An approximately equal rate of cooling (3 to 4 hours unless otherwise noted) was assured by allowing all the soap mixtures to chill in a standard container (an oil extraction flask of 150 cc. capacity). The cooling mixtures were *not* stirred, for in passing from the solution of soap in water to that of water in soap, the emulsion zones of hydrated soap-in-soap water followed by that of soap water-in-hydrated soap are passed, and stirring would obviously break the gradually devel-

[22] Martin H. Fischer: Kolloid-Zeitschr. *34*, 140 (1924).

[23] Martin H. Fischer: Science, *49*, 615 (1919); Chemical Engineer, *27*, 271 (1919); Soaps and Proteins, 77, New York (1921).

oping external phase of hydrated soap to which, in our minds, the initial and marked increase in electrical resistance is due.[24]

What happens for a series of sodium soaps is illustrated in Fig. 22, the curves from left to right being constructed from the data contained respectively in Tables XXV, XXVI, XXVII, XXVIII, XXIX and XXX. The sodium chlorid curve is for purposes of control to illustrate the electrical behavior of an ordinary strong electrolyte. The sodium acetate curve above it

TABLE XXV.—*Electrical resistance of a ½ m sodium stearate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
79	4.00	59	12.22
72	4.16	58.5	13.80
69	4.51	57.5	16.66
67.5	4.69	57	17.00
66	4.69	55.5	19.95
63	4.88	55	21.20
62	4.93	54	22.53
60.5	5.19	40	48.38
60	5.41	36.3	52.04
60	5.75	33	55.72
60.3	6.25	33	58.22
60.5	6.50	32.5	56.38
60	9.78	31.5	58.22
60	10.83		

shows how this "soap," as the salt of a weak acid with a strong base, is not only a poorer conductor of electricity but, as a material which with water does *not* yield a colloid system, also shows no break in its gradual ascent. The horizontal portions of the laurate, myristate, palmitate and stearate curves all lie well above the acetate curve, the differences tending to become increasingly exaggerated at the lower temperatures. These resistances are definitely higher than might be expected on the assumption that the higher soaps are *merely* still weaker elec-

[24] It seems to us that through the failure to observe some such precaution is due J. W. McBAIN'S observation that gels do not register a definitely higher electrical resistance than sols.

trolytes in aqueous solution. Deviations of this type from the ordinary laws of the dilute solutions have made various students of the problem since the days of F. KRAFFT[25] declare the mixtures "colloid." *The degree of such deviation from the anticipated electrical resistance is the measure, to our minds, of the amount of the system which is not in ordinary solution in water but present as water dissolved in soap (hydrated soap).* With falling temperature this fraction must obviously increase. As soon as it becomes sufficient to constitute the main portion of the

TABLE XXVI.—*Electrical resistance of a ½ m sodium palmitate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
85.5	3.30	52	10.62
84	3.34	51	12.50
83	3.38	51	16.91
70	3.84	50.5	23.46
62	4.34	50	29.77
56	4.61	49	38.19
53	4.86	47.5	48.02
52.2	5.30	46.5	57.11
52.2	5.86	45.5	66.08
52.2	6.68	45	70.35
52	8.15	43	80.83

soap/water system (as soon as it becomes the external phase and the system gels) it was to be expected that a sudden increase in electrical resistance should register itself, since a solution of the water in the soap (hydrated soap) is a poorer conductor of electricity than a solution of soap in water. The perpendicular rises in the later portions of the several curves show that this change actually occurs, such rises being registered at successively higher temperatures as we pass from the laurate toward the stearate. This is the same order in which the hydration capacity of the several soaps increases.

The potassium soaps of the acetic series are more soluble *in* water than the corresponding sodium soaps. It was to be ex-

[25] F. KRAFFT and H. WIGLOW: Ber. d. deut. chem. Gesellsch., *28*, 2573 (1895).

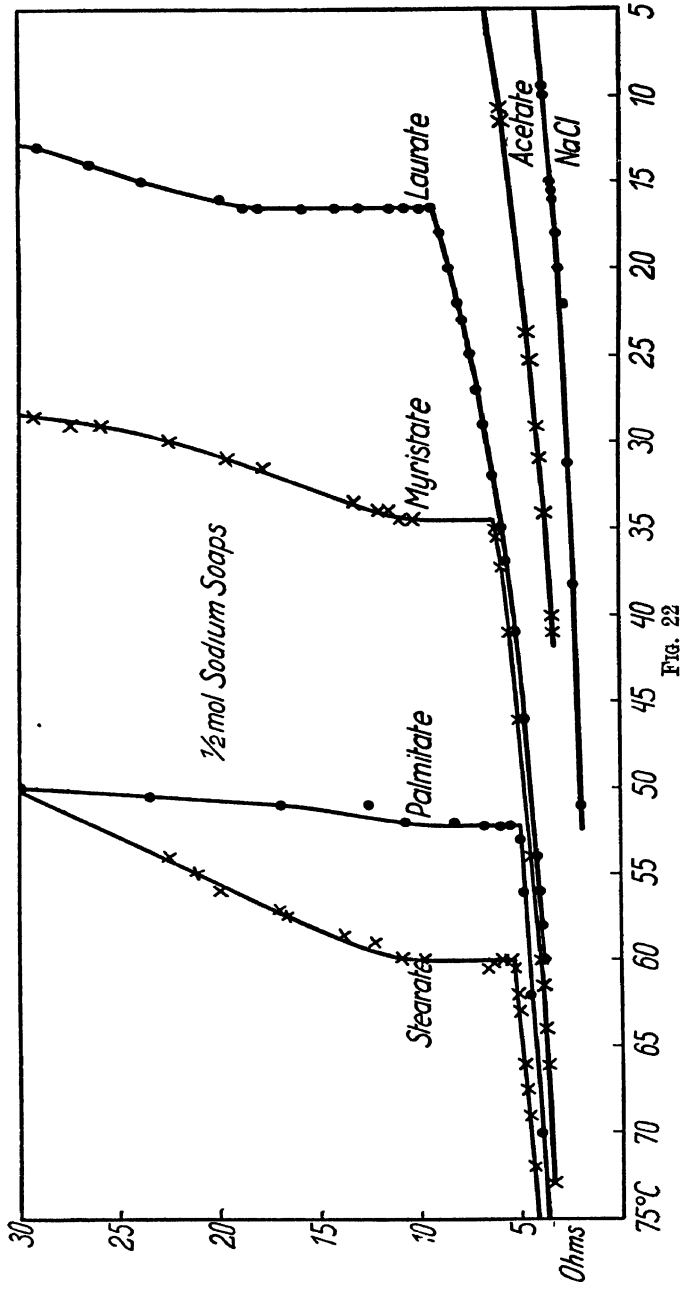

½ mol Sodium Soaps
Laurate
Myristate
Palmitate
Stearate
Acetate
NaCl
Ohms
75°C
30
25
20
15
10
5
5
10
15
20
25
30
35
40
45
50
55
60
65
70

FIG. 22

TABLE XXVII.—*Electrical resistance of a ½ m sodium myristate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
73	3.38	34	12.02
66	3.52	34	12.52
64	3.66	33.5	13.30
61.5	3.81	32.5	14.12
60	3.89	31.5	17.96
54	4.31	31	18.70
46	5.06	30	22.50
41	5.52	30	22.61
40	5.52	29	26.02
37.5	5.86	29	27.41
35.5	6.23	28.5	29.34
35	6.28	28	30.55
35	6.36	26.5	34.24
34.5	6.36	26	35.24
34.5	10.38	26	35.24
34.5	11.08	26	39.93
34	11.54	26	39.20

TABLE XXVIII.—*Electrical resistance of a ½ m sodium laurate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
60	3.47	16.5	9.47
58	3.86	16.5	9.99
56	3.97	16.5	10.72
56	4.03	16.5	11.49
54	4.33	16.5	13.05
46	4.88	16.5	14.18
41	5.30	16.5	15.90
37	5.80	16.5	18.09
35	6.00	16.5	18.83
32	6.49	16	20.40
29	6.89	15	23.91
27	7.14	14	26.51
25	7.58	13	29.14
23	7.92	12.5	32.63
22	8.15	12	36.02
20	8.55	11.5	40.24
18	8.98		

pected, therefore, other conditions being the same, that the sharp changes in electrical resistance in a series of cooling potassium soaps should occur at decidedly lower temperatures than in the case of the corresponding sodium soaps. This fact finds expression in Fig. 23 constructed from the data contained in Tables

TABLE XXIX.—*Electrical resistance of a ½ m sodium acetate/ water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
41	3.25	25	4.50
40	3.31	25	4.42
34	3.66	23.5	4.60
31	4.05	11.5	5.87
29	3.97	10.6	5.87
25.3	4.40		

TABLE XXX.—*Electrical resistance of a ½ m sodium chlorid/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
51	1.84	17	3.31
38.3	2.21	16	3.31
31.3	2.49	15.5	3.38
22	2.76	15	3.45
20	3.00	10	3.66
20	3.06	9.5	3.74
18	3.18		

XXXI, XXXII, XXXIII, XXXIV and XXXV. The potassium chlorid curve is again introduced for purposes of control. The first portions of all the potassium soap curves lie well above this, but the group as a whole lies definitely lower than the corresponding sodium soap curves. So far as the acute ascents in electrical resistance are concerned, the whole potassium series lies to the right of the corresponding sodium soaps.

The sodium soaps of the acetic series with water yield systems which are definitely solid. Diagrammatically their internal arrangement is therefore that of B of Fig. 2. The potassium

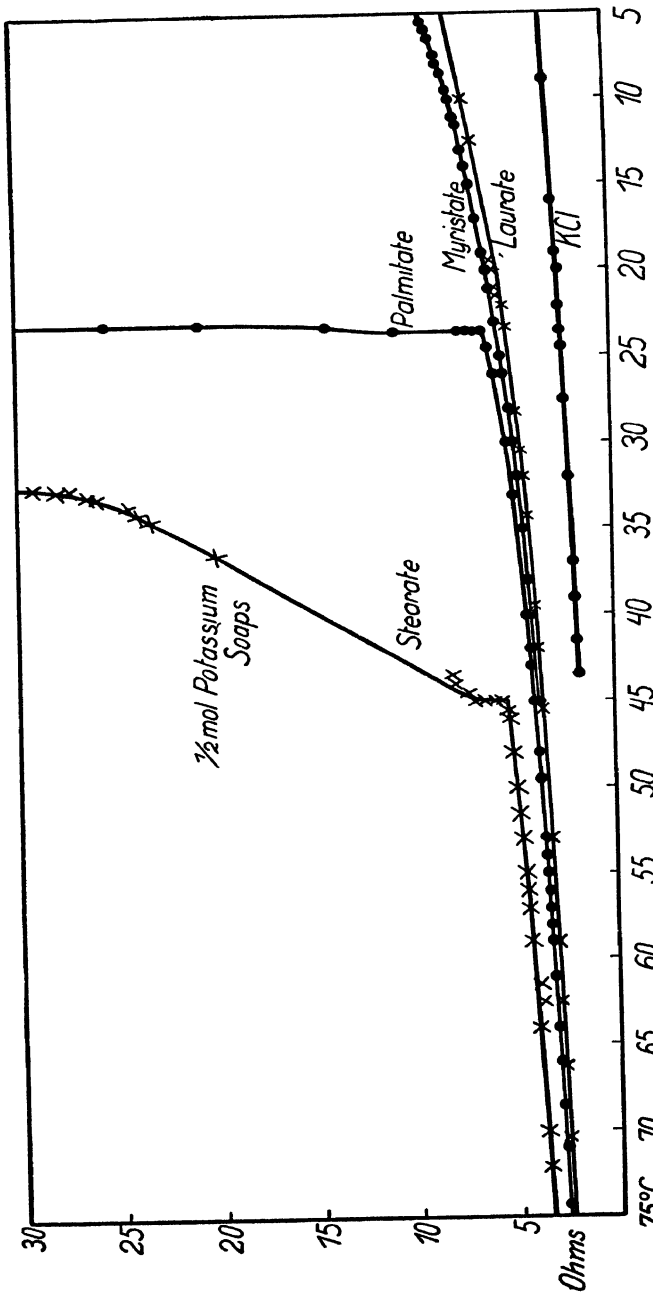

Palmitate
Myristate
Laurate
KCl
½mol Potassium Soaps
Stearate
Ohms
75°C
30
25
20
15
10
5
5
10
15
20
25
30
35
40
45
50
55
60
65
70

FIG. 23

soaps of the same series with water yield mixtures best described as semi-solid (the mixtures are "crystalline" but the crystals are so soft or "liquid" that they are easily distorted). In the case of the potassium soaps of the lower fatty acids (below lauric) the cooled systems are thickly viscid and only slowly

TABLE XXXI.—*Electrical resistance of a ½ m potassium stearate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
87	3.00	45	5.70
86	3.12	45	6.00
82.5	3.25	45	6.00
80	3.38	45	6.50
79	3.31	45	7.04
78	3.45	44.5	7.04
72	3.52	44.5	7.33
70	3.66	44	7.63
66	4.14	44	7.95
64	3.97	43.5	8.11
62.5	3.81	36.5	19.86
61.5	3.97	36.5	20.00
60	3.97	34.5	23.47
59	4.50	34	23.95
59	4.24	33.5	24.44
57	4.24	33	25.97
56	4.42	33	26.51
53	4.69	32.5	27.39
51.5	4.88	32.5	27.62
50	4.94	32.5	28.10
48	5.13	32.5	29.25
47	5.30	32.3	29.84
46	5.30	32	32.73
45.5	5.30	31	37.33
45	5.30	29	45.58
45	5.52		

become definitely solid and crystalline. The changes in electrical resistance described for the sodium soap/water systems may therefore be taken as characteristic of lyophilic colloids having the composition *solid with liquid* and with these systems may be placed the potassium soap/water systems in the case of the

higher fatty acids. But the potassium soap/water systems of the lower fatty acids already approximate lyophilic colloid systems of the type liquid with liquid.

What now is the electrical behavior of cooling lyophilic colloid systems which are definitely of the composition *liquid with liquid?* We chose for the study of this question sodium oleate and potas-

TABLE XXXII.—*Electrical resistance of a ½ m potassium palmitate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
85	2.32	33	4.80
83	2.35	30	5.20
82	2.37	26	5.75
80	2.46	24.5	6.11
78	2.53	24	6.31
77	2.51	23.5	6.52
75	2.57	23.5	7.13
73	2.63	23.5	7.51
71	2.68	23.5	10.77
68.5	2.81	23.2	14.23
66	2.87	23	20.64
64	2.94	23	25.45
61	3.06	23	32.08
59	3.15	23	40.60
58	3.19	22.6	56.42
56	3.29	22.5	63.89
55	3.40	22.5	71.86
54	3.45	22.5	79.53
53	3.45	22.2	88.14
49.5	3.66	22	93.67
48	3.75	22	98.01
45	3.92	21.8	108.33
43	4.09	21.5	115.05
42	4.17	21.2	119.78
40	4.25		

sium oleate with water. The findings are illustrated in Fig. 24 and Tables XXXVI and XXXVII. At half molar concentration the sodium oleate curve lies well above the potassium oleate curve and both above the resistances registered by the solution of any ordinary weak electrolyte like sodium acetate. At the

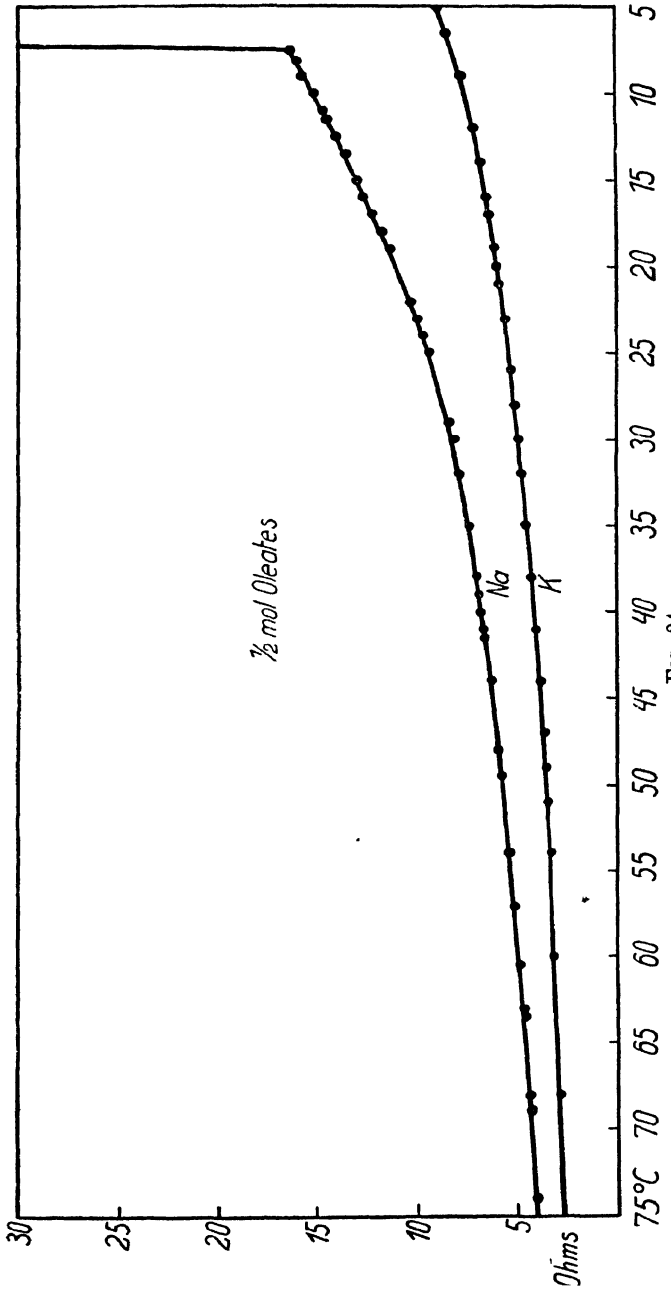

½ mol Oleates
Na
K
Ohms
30
25
20
15
10
5
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75°C

Fig. 24

higher temperatures the oleates show a slightly lower resistance than the corresponding stearates. With falling temperature the resistance of both oleates, however, ascends more steeply than the corresponding first portions of the acetic series soaps. This rapid rise in electrical resistance is comparable, we hold, to that observable when a liquid system of phenol and water changes,

TABLE XXXIII.—*Electrical resistance of a ½ m potassium myristate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
75	2.46	11	7.50
65	2.81	10	7.65
56	3.13	9.5	7.88
49	3.40	8.5	8.08
45	3.66	8	8.22
40	4.04	6.5	8.69
38	4.17	6	8.88
35	4.43	5.5	9.00
32	4.61	5	9.16
30	4.80	4.5	9.28
28	4.96	3.5	9.70
26	5.24	2.5	10.10
25	5.35	2	10.29
23	5.57	1	10.52
21	5.84	.5	11.23
20	5.98	.5	11.55
19	6.23	.5	12.66
17	6.49	.5	42.16
15	6.76	.5	42.86
14	6.90	.5	57.24
13	7.13	.5	63.78
11.5	7.34		

with lowering of temperatures, from a solution of the phenol-in-water to one of the water-in-phenol (see Fig. 21).

A half molar sodium oleate/water system loses its optical homogeneity and becomes milky at about 7.5° C. At this temperature crystals appear and the total system gradually goes solid. We deal in this region, obviously, with the transformation of a liquid-liquid hydrated colloid mixture into a liquid-solid

TABLE XXXIV.—*Electrical resistance of a ½ m potassium laurate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
79	2.40	34.3	4.31
76.5	2.45	32	4.50
74.5	2.50	30.5	4.55
70.5	2.60	30.5	4.70
66.3	2.71	28.3	4.70
62.5	2.88	23.3	5.20
59	3.12	22	5.30
57	3.25	21.5	5.63
54	3.31	21	5.75
53	3.38	20	5.86
48	3.52	19.5	5.98
45.5	3.59	12.5	6.76
42	3.81	10	7.19
39.5	3.89		

hydrated one and would expect a new and further rise in resistance. That such actually occurs may be observed in the final portion of the sodium oleate curve and the final electrical resistance values of Table XXXVI. Potassium oleate does not go solid before 0° C. is reached; its ascending curve, therefore, runs smoothly to the edge of the diagram.

We wish now, for purposes which will appear later, to indicate what happens to the electrical resistance of soap/water systems as these pass through the gelation realm, depending upon

TABLE XXXV.—*Electrical resistance of a ½ m potassium chlorid/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
51	1.63	24.5	2.37
43.5	1.71	23.5	2.44
41.5	1.77	22	2.44
39	1.80	20	2.49
37	1.88	19	2.57
32	2.04	16	2.70
27.5	2.16	9	2.76

whether the initial system is more or less concentrated. In the observations thus far described all the soap/water systems were half molar. If in the case of potassium laurate the concentration is raised to molar or double molar the electrical resistance *is lowered* throughout, the curves showing the changes in electrical resistance with dropping temperature indicated in the three lower

TABLE XXXVI.—*Electrical resistance of a ½ m sodium oleate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
78.5	3.72	30	8.11
78	3.81	29	8.41
74	4.05	25	9.41
69	4.29	24	9.72
68	4.34	23	10.00
63.5	4.56	22	10.32
63	4.65	19	11.36
60.5	4.86	18	11.73
57	5.10	17	12.17
54	5.37	16	12.72
49.5	5.82	15	12.98
48	6.03	13.5	13.52
44	6.36	12.5	14.09
41.5	6.70	11.5	14.50
41	6.76	11	14.63
40	6.90	10	15.12
39	7.04	9	15.77
38	7.13	8	15.97
35	7.34	7.5	16.31
32	7.72	7	44.05
32	7.85	7	44.16

curves of Fig. 25 and in Tables XXXIV, XXXVIII and XXXIX. Here, obviously, we deal with an increase in the conducting element with increase in the concentration of the "colloid" (just as we deal with improved conductivity as the amount of an electrolyte in any dilute solution is increased). When, however, a soap like sodium stearate is used these changes are *reversed.* The electrical resistance of a molar "solution" of this soap is greater than that of a half molar (as shown in the

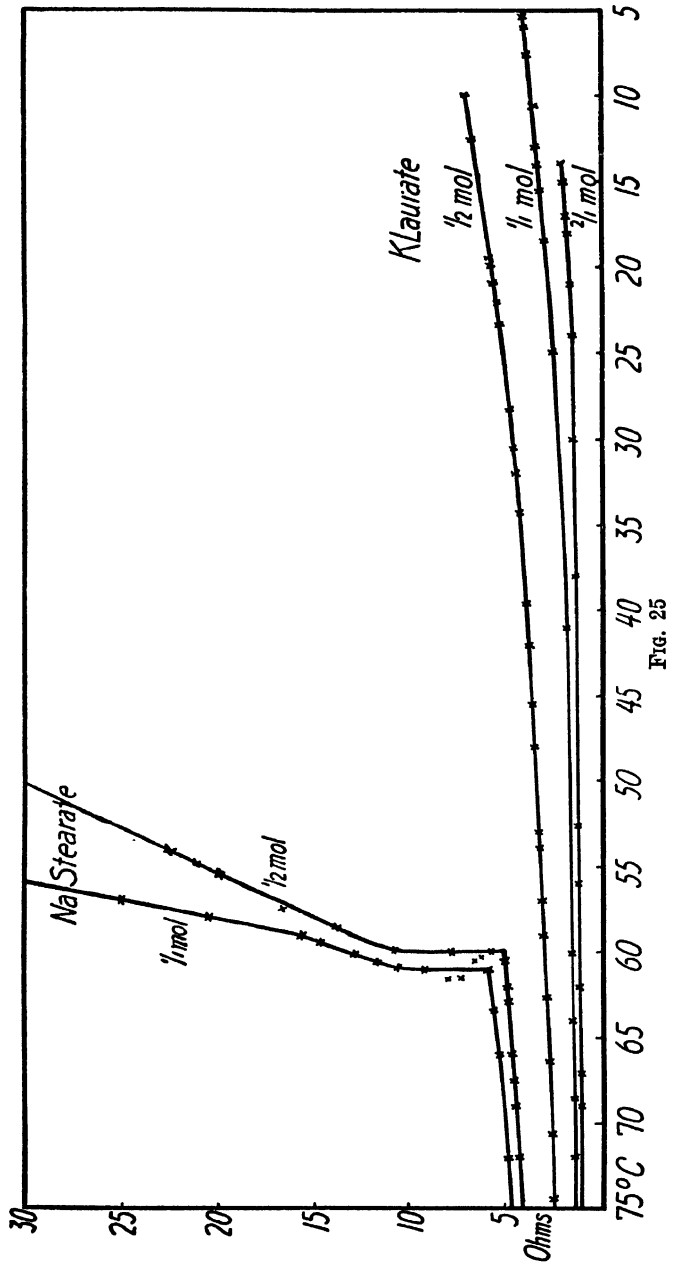

Na Stearate
1/1 mol
1/2 mol
K Laurate
1/2 mol
1/4 mol
1/8 mol
30
25
20
15
10
5
Ohms
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75°C

FIG. 25

TABLE XXXVII.—*Electrical resistance of a ½ m potassium oleate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
59	2.93	21	5.88
57	3.20	20.5	5.88
56	3.24	19.5	5.88
53	3.38	19	6.12
44.5	3.69	18.5	6.12
40	4.00	18	6.19
38.5	4.16	17.5	6.35
35	4.38	17	6.50
32	4.60	12.5	7.04
28.5	4.79	12.5	7.14
27	5.04	10.5	7.38
25	5.19	9	7.89
24.5	5.36	8	8.21
23.5	5.52	7	8.38
23.5	5.38	6	8.55
22	5.71	3.5	9.01

two upper curves of Fig. 25 and in Tables XXV and XL) and the electrical resistance rises earlier when gelation begins. We hold that these facts evidence the existence from the start of a

TABLE XXXVIII.—*Electrical resistance of a 1/1 m potassium laurate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
84	1.22	13	3.38
75.5	1.33	10.5	3.45
72	1.38	9	3.52
68.5	1.41	8.3	3.66
64	1.50	7.5	3.81
60	1.50	6	3.89
41	1.70	5.5	4.22
25.5	2.34	3	4.25
25	2.54	2	4.25
18.5	3.00	1	4.43
15.5	3.12	0.5	4.80
14	3.10		

TABLE XXXIX.—*Electrical resistance of a 2/1 m potassium laurate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
90.5	0.88	56	1.22
88	0.92	52.5	1.22
85	1.04	38	1.32
83	1.06	30	1.38
79	1.08	24	1.43
75.5	1.10	21	1.50
72	1.10	19	1.57
69	1.10	18	1.63
67	1.10	17	1.77
64	1.12	15.5	1.92
62	1.17	15	2.00

larger fraction of the poorer conducting phase (hydrated soap) in the soap/water system and its earlier appearance as the external phase when the soap is in high concentration than when present in a lower one.

TABLE XL.—*Electrical resistance of a 1/1 m sodium stearate/water system with falling temperature*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
87	3.95	59.5	14.68
84.5	4.25	59	15.65
81	4.25	58	20.45
78	4.48	57	25.00
75	4.61	56	30.55
72	4.81	55	37.50
66.5	5.21	54	42.56
63.5	5.65	50	65.90
61.5	7.33	49	67.25
61.5	7.95	47	73.73
61	8.63	45	77.91
61	9.18	44	78.93
61	10.66	40	88.37
60.5	11.64	31	122.83
60	12.75	29	127.18

B. The System Gelatin/Water[26]

The gelatin employed was an Eastman Kodak Company product of an ash content of 0.04 percent, rather rich in diffusible nitrogen (24 mgms. per 20 gms. of the gelatin as determined by SCHRYVER'S method) and of low setting power (almost 3 per cent being required to obtain a non-flowing jelly at 20° C.). We used this particular material because it is of the type upon which many of the more recent studies of the colloid-chemical behavior of gelatin have been made in the United States.

The same electrodes, of the constant 0.125, used in the previously described experiments on soaps were employed.

The study of these gelatin/water systems was carried out, in all instances, by introducing weighed amounts of gelatin into a standard cooling vessel, adding the necessary amount of water and bringing about "solution" in a water bath at a temperature below 50° C. When electrolytes were employed, these were added *after* such "solution" had been effected. The mixture to be studied was then quickly heated to 90°, the electrodes and thermometer introduced and the whole plunged into a circulating ice-water bath. The colloid mixture itself, of course, was not stirred. To chill the mixture in our standard containers from 90° to 2° required about an hour and a half. This rate is the standard one for all the experiments described. When the cooling was carried out more slowly the beginning and end values of our curves were the same, though in their middle portions they were somewhat less convex toward the base.

Fig. 26 and Tables XLI, XLII, XLIII, XLIV show how the electrical resistance of a gelatin/water mixture increases with falling temperature. The findings are plotted for four different concentrations of the pure gelatin.

It is first to be noted that, for this gelatin and within the concentrations employed, there is a *decrease* in resistance with every increase in the concentration, the low concentration gelatin/water mixture lying highest in Fig. 26, the high concentration, lowest. In this regard, these gelatin/water systems are to be compared with soap/water systems of the type potassium laurate/water in which, also, increase in the concentration of the

[26] MARTIN H. FISCHER: Kolloid-Zeitschr. *35*, 138 (1924).

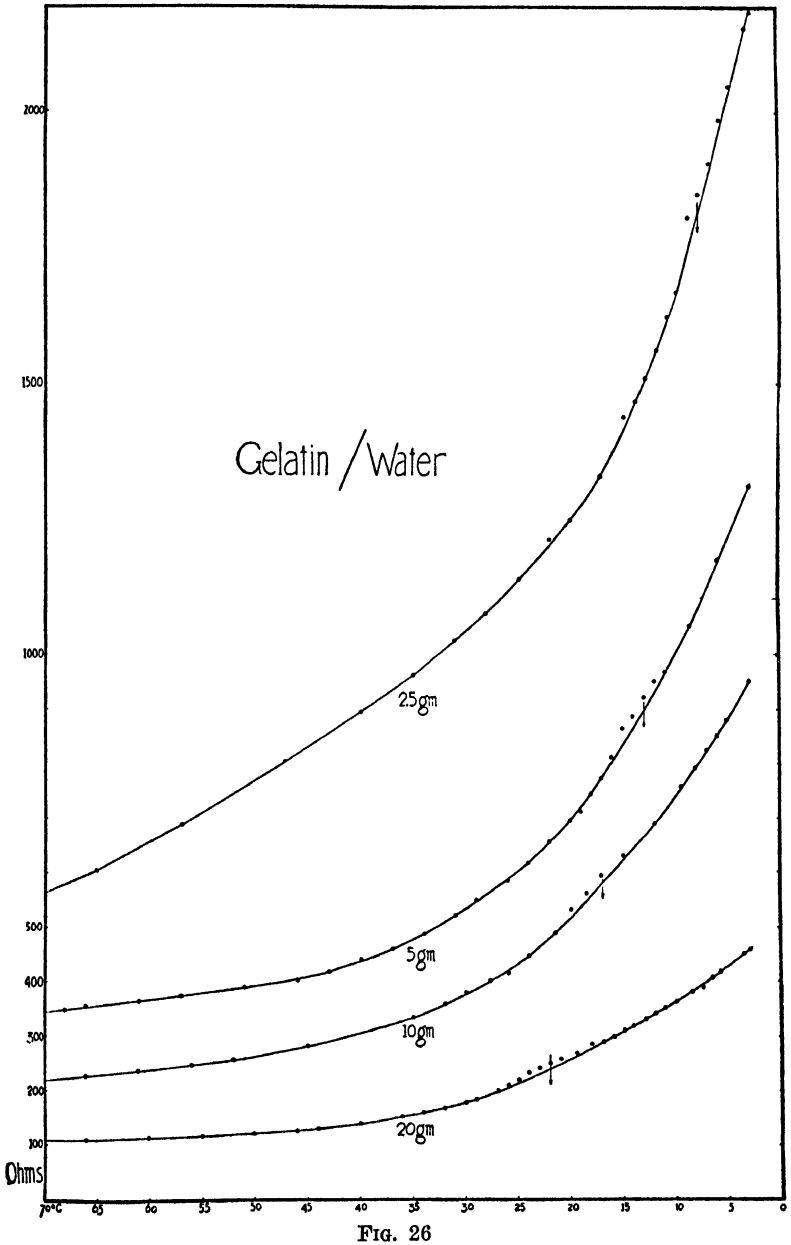

Gelatin / Water
2.5gm
5gm
10gm
20gm
Ohms
2000
1500
1000
500
400
300
200
100
70°C
65
60
55
50
45
40
35
30
25
20
15
10
5
0

FIG. 26

soap for any given temperature is followed by a lowering of the electrical resistance of the system (due, we think, to the ready solubility of this soap *in* the water); the gelatin/water system does *not* behave like a sodium stearate/water system in which every increase in concentration for a given temperature leads to an increase in electrical resistance[27] (due, in our opinion, to the increase in the phase, water-dissolved-in-soap, with its higher electrical resistance). The second point of note in Fig.

TABLE XLI.—*Electrical resistance of 2.5 gms. ashless gelatin + 100 cc. water at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° C.		° C.	
75	557	15	1438
74	564	14	1468
73	566	13	1508
72	571	12	1558
65	604	11	1619
57	691	10	1667
47	803	9	1805
40	896	8	1848
35	962	*7	1904
31	1025	6	1988
28	1073	5	2051
25	1140	3.5	2159
22	1212	3	2189
20	1249	2.5	2231
17	1327		

* Solid.

26 is the remarkably acute increase in electrical resistance as the gelation realm is approached. The resistance curve of any ordinary electrolyte dissolved in water shows no such sharp turn upwards with falling temperature. This abrupt change, to our minds, is to be accepted as proof that *the resistance increases as the system changes from the better conducting "solution" of gelatin-in-water to the poorer one of water-in-gelatin.*

Fig. 27 and Tables XLV, XLVI and XLVII show the effects of falling temperature upon the electrical resistance of an acid-

[27] See page 64.

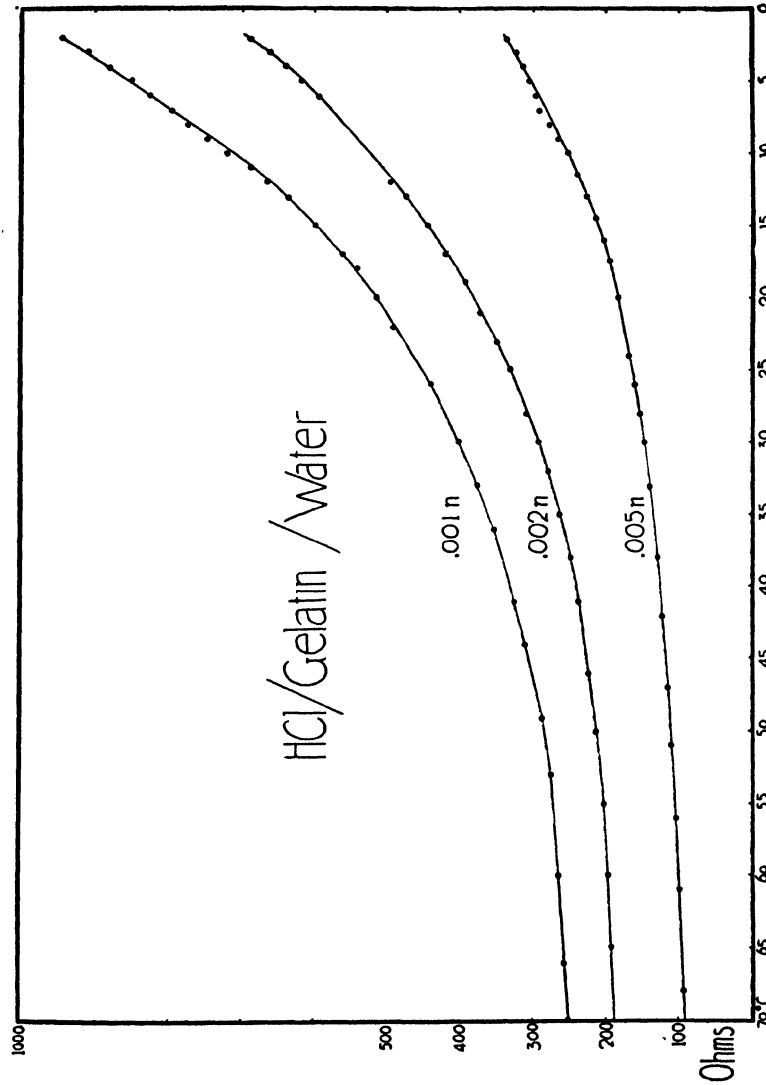

HCl/Gelatin /Water
.001 n
.002 n
.005 n
Ohms
1000
500
400
300
200
100
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70°C

FIG. 27

gelatin/water system. As we believe that present day methods do not allow us to know just when a protein has been "neutralized" by an acid,[28] we detail the effects of adding three different amounts of hydrochloric acid to a standard gelatin/water mixture.

TABLE XLII.—*Electrical resistance of 5 gms. ashless gelatin + 100 cc. water at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
74.5	320	22	657
73	326	20	696
72	331	19	714
68	349	18	744
66	355	17	772
61	362	16	812
57	373	15	866
51	390	14	889
46	406	*13	924
43	417	12	954
40	440	11	971
37	462	8.5	1054
34	488	7	1123
31	522	6	1177
29	548	5	1218
26	585	4	1225
24	616	3	1312

* Solid.

The three curves of Fig. 27 need to be compared with the uppermost one of Fig. 26. It will be observed, first, that the electrical resistance is, in all instances, lowered through the addition of the acid and this in increasing amount with increase in the concentration of the added acid. The resistance does not however fall even approximately to the level of that shown by simple solutions of the same amounts of acid in comparable volumes of pure water. This fact can be understood in only one of two ways, either as proof of the old contention of S.

[28] MARTIN H. FISCHER: Science, *49*, 615 (1919); Chemical Engineer, *27*, 271 (1919); Soaps and Proteins, *77*, 228, New York (1921); see p. 115 and 225.

BUGARSZKY and L. LIEBERMANN[29] that acids unite with protein; or by saying that gelatin-water (hydrated gelatin) is a different "solvent" for acid than pure water. We consider the formation of an acid proteinate from the original "neutral" gelatin the major factor. Such acid proteinates are more soluble in water than neutral protein[30] which accounts for the better general con-

TABLE XLIII.—*Electrical resistance of 10 gms. ashless gelatin + 100 cc. water at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
80	211	26	426
78	214	24	447
76	216	21.5	490
72	219	20	533
66	225	18.5	562
61	232	*17	594
56	243	15	631
52	253	12	692
48	254	9.5	759
45	281	8	792
42	296	7	826
35	333	6	851
32	359	5	881
30	382	3	953
28	404		

* Solid.

ductivity of these systems over the corresponding neutral gelatin/water systems. But with lowering of temperature, gelation comes about with increasing formation of the phase water-dissolved-in-acid-gelatin, which explains the large swings upward of the curves of Fig. 27 in the low temperature regions of the diagram.

The effects of acids upon the colloid-chemical behavior of protein (its swelling, "solution," etc.) indicate that such are *not* a

[29] S. BUGARSZKY and L. LIEBERMANN: Pflüger's Arch., *72*, 51 (1898).

[30] MARTIN H. FISCHER: Nephritis, 9, New York (1912); Œdema and Nephritis, 3rd Ed., 508, New York (1921).

simple function of their hydrogen-ion concentration but specific. Presumably, different proteinates are formed, each possessed of a different solubility in water and for water. It was therefore to be expected that the electrical conductivity of acid/protein/water systems would also show a difference depending upon the kind of acid used. The curves of Fig. 28 and Tables XLVIII,

TABLE XLIV.—*Electrical resistance of 20 gms. ashless gelatin + 100 cc. water at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° C.		° C.	
80	100	23	242
78	104	*22	251
72	107	21	259
66	110	19.5	269
60	112	18	286
55	114	17	292
50	120	16	301
46	126	15	313
44	130	14	318
40	140	13	330
36	153	12	343
34	160	11	352
32	168	10	363
30	179	8.5	382
29	185	7.5	389
27	201	6.5	406
26	210	5.75	416
25	220	3.5	450
24	233	3	460

* Solid.

XLIX and L show that this is the case. The hydrochloric acid curve has been redrawn from the middle curve of Fig. 27 (Table XLVI) for purposes of comparison. It will be noted that the sulphuric acid curve lies definitely above this while still higher lie the curves for acetic and lactic acids.

Attention should be drawn to the peculiarly high values of the resistance in the low temperature realm from the lactic and acetic acid proteinates. These proteinates, obviously, are peculiarly

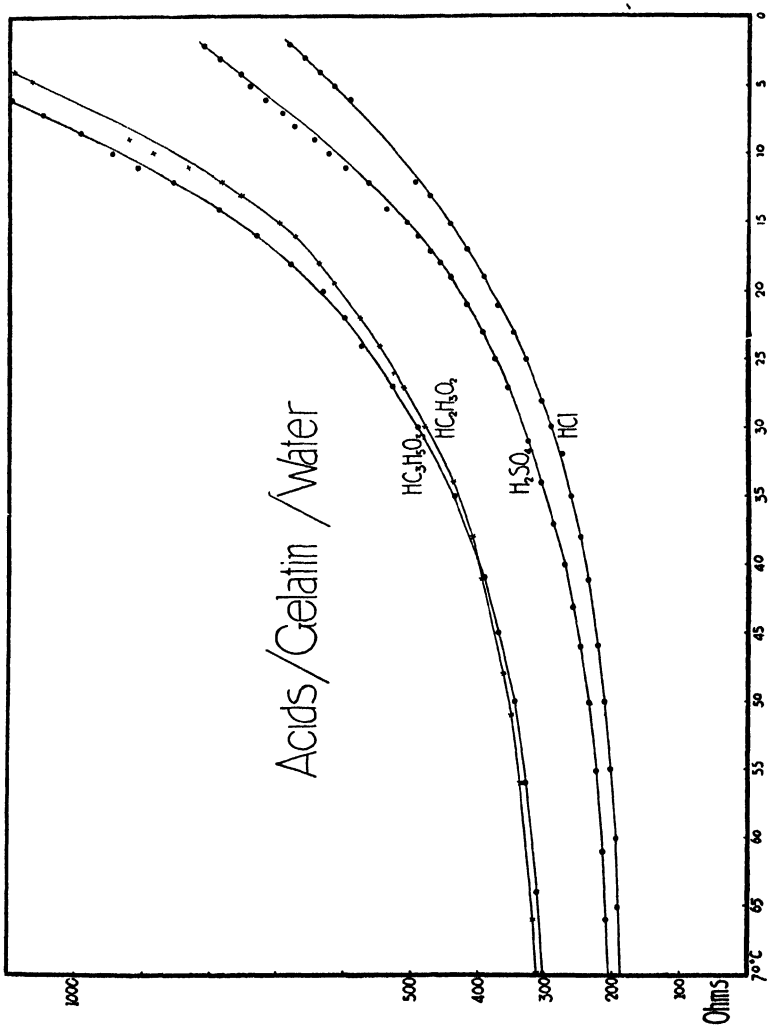

Acids/Gelatin /Water
$HC_3H_5O_2$
$HC_2H_3O_2$
H_2SO_4
HCl
Ohms
1000
500
400
300
200
100
70°C
65
60
55
50
45
40
35
30
25
20
15
10
5
0

FIG. 28

TABLE XLV.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 99 cc. water + 1 cc. 1/10 n hydrochloric acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
79	241	18	544
76.5	245	17	563
70	253	15	600
66	256	13	637
60	262	12	666
54	273	11	689
49	288	10	721
44	312	9	748
41	326	8	775
36	354	7	795
33	378	6	826
30	404	5	853
26	441	4	881
24	467	3	911
22	494	2	943
20	517		

TABLE XLVI.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n hydrochloric acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
78	180	23	351
77	181	21	375
76	182	19	395
71	189	17	421
65	191	15	445
60	195	13	476
55	202	12	497
50	213	11	519
46	224	9	546
41	240	8	572
38	249	6	594
35	255	5	620
32	280	4	640
30	294	3	662
28	310	2	685
25	332		

TABLE XLVII.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 95 cc. water + 5 cc. 1/10 n hydrochloric acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
79	87	20	183
78	87	17.5	196
73	91	16	205
68	91	14.5	214
61	98	13	228
56	102	11.5	240
51	110	10	254
47	115	9	266
42	121	8	279
38	129	7	291
33	141	6	298
30	148	5	305
28	155	4	314
26	162	3	322
24	170	2	336

TABLE XLVIII.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n lactic acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
78	294	20	635
77	296	18	685
72	304	16	734
64	313	14	790
56	330	12	858
50	348	11	911
45	372	10	949
41	395	8.5	997
38	413	7	1050
35	437	6	1098
30	497	5	1142
27	533	4	1179
24	578	3	1208
22	603	2.5	1249

TABLE XLIX.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n acetic acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
80	288	24	552
77.5	294	22	581
76	296	19.5	620
74	301	18	640
70	313	16	677
66	317	15	701
62	322	13	757
56	332	12	785
51	353	11	836
47	367	10	887
42	392	9	924
38	412	4.5	1066
34	441	4	1090
30	485	3	1116
27	514	2	1152
26	530		

TABLE L.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n sulphuric acid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
80	192	19	445
78	194	18	460
74	202	17	476
70	206	16	494
66	208	15	509
61	213	13	541
55	225	12	566
50	237	11	600
46	250	10	627
43	262	9	648
40	274	8	677
37	291	7	697
34	310	6	721
31	328	5	743
27	359	4	757
25	380	3	788
23	397	2	810
21	421		

TABLE LI.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 94 cc. water + 6 cc. 1/30 n calcium hydroxid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
79	259	17.5	581
77	259	16	603
67	266	15	623
62	271	13.5	655
52	293	11	717
47	311	10	757
44	324	9	785
40	342	8	820
37	362	7	864
34	391	6	899
31	412	5	930
28	439	4	983
25	476	3	1026
22	509	2	1050
20	535		

TABLE LII.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n sodium hydroxid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
80	220	22	485
79	221	18.5	533
75	227	17	561
70	234	16	575
65	247	15	603
60	248	13	644
54	282	11	689
50	306	10	722
45	322	9	757
40	352	7.5	810
37	368	6	847
33	393	5	869
30	406	4	893
28	423	3	924
24	458	2	956

TABLE LIII.—*Electrical resistance of the system 2.5 gms. ashless gelatin + 98 cc. water + 2 cc. 1/10 n potassium hydroxid at different temperatures*

Temperature	Resistance in ohms	Temperature	Resistance in ohms
° *C.*		° *C.*	
80	185	21	419
78	187	19	435
72	192	17	449
66	203	15	471
61	225	12.5	504
56	240	11	519
51	259	10	530
46	282	9	543
42	295	8	572
39	308	7	594
36	321	6	610
33	341	5	626
30	356	4	647
26	382	3	666
24	395	2	693

rich in the phase, water-dissolved-in-acid-proteinate and low in the phase proteinate-dissolved-in-water, a finding which harmonizes well not only with laboratory studies on the effects of different acids on the swelling of pure protein but with the empirically well known technical fact that in tanning, for example, acetic and lactic acids produce the greatest swelling of hides with the lowest tendency to make them "go into solution."

Fig. 29 and Tables LI, LII, and LIII show the effects of three different alkalies upon the electrical resistance of a cooling gelatin/water system. While these three alkalies are about equally "strong," it is noteworthy that calcium hydroxid reduces the resistance less than sodium hydroxid and this less than potassium hydroxid. The rapid increase in electrical resistance with lowering of temperature in the case of these three alkali/protein/water systems is again self-evident.

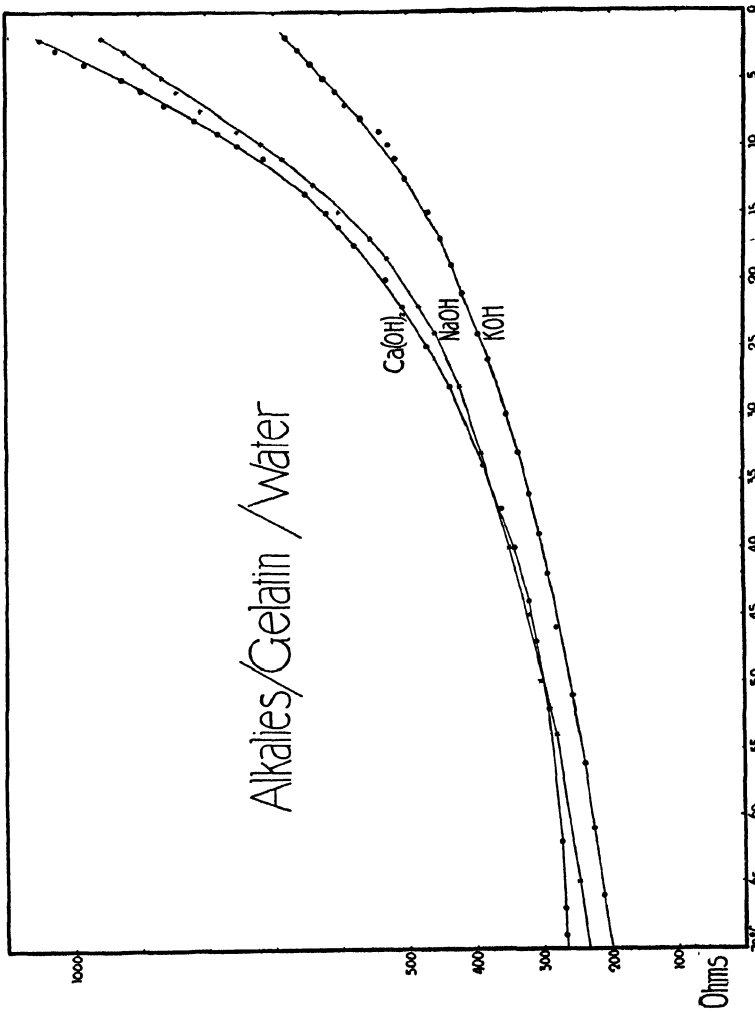

Alkalies/Gelatin /Water
Ca(OH)2
NaOH
KOH
Ohms
1000
500
400
300
200
100
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70°C

Fig. 29

C. The System Casein/Water[31]

The lyophilic colloid systems which may be made of various casein derivatives with water, exhibit, with changes in temperature, the same change in electrical resistance (an enormous and abrupt increase on being cooled) just described for gelatin/water, soap/water, phenol/water, and quinolin/water systems. This is evidence, in a second protein, for our general theory of the lyophilic colloid state according to which these systems change progressively, with falling temperature, from what is, at the higher temperature, essentially a solution of x-in-water to what, at the lower, is essentially a solution of water-in-x.

We proceeded in these experiments on casein as in the previously described ones with gelatin. A commercial product (Harris) low in salts was used. As pure casein is practically unsolvated in water, only combinations of this with alkali or acid could be used to obtain the lyophilic, gelatinizing systems necessary.

All the mixtures used were prepared in exactly the same fashion. The casein was weighed into glass-stoppered cylinders of standard form and size and to it was added the necessary standard solution of acid or alkali. The mixtures were allowed to stand in a refrigerator for twenty-four hours with occasional stirring to hasten "solution." Care was taken to avoid admixture with air. When a fairly homogeneous mixture had been obtained, the cylinders were stirred and heated to 100° in a water bath, until translucent systems were obtained; and the electrodes and a thermometer were introduced. The entire apparatus was then placed in a circulating ice-water bath, though the colloid solution itself was, of course, *not* stirred. About three hours were required to bring these solutions from the temperature of a hot water bath to 2° C. Careful checks showed that slower cooling did not appreciably influence our final values.

Electrical resistance was measured as before with a pair of fixed, platinized platinum electrodes (of the constant 0.109) frequently tested against 1/50 n potassium chlorid to make sure that they had suffered no change.

[31] MARTIN H. FISCHER and MARIAN O. HOOKER: Kolloid-Zeitschr. *23*, 200.

Fig. 30 and Table LIV show how the electrical resistance of four different concentrations of a KOH/casein/water system increases with falling temperature. The amount of potassium hydroxid added to the casein in each of these instances is that

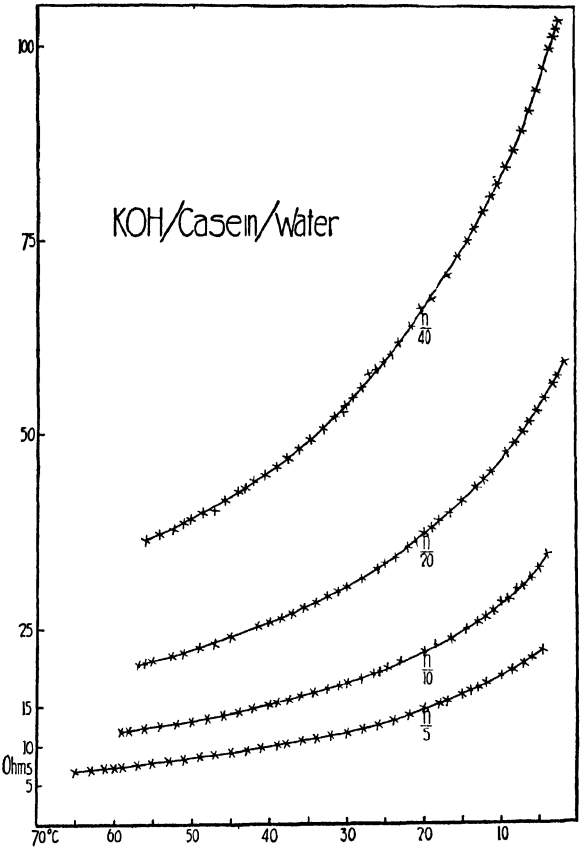


FIG. 30

commonly accepted as necessary for its neutralization. If the value is taken to be correct (we ourselves question whether such neutralization equivalents as determined for definitely colloid systems are entirely trustworthy[32]) then we may say that the curves cover the behavior of four different concentrations of a potassium caseinate/water system. The electrical resistance of

[32] See footnote, p. 72.

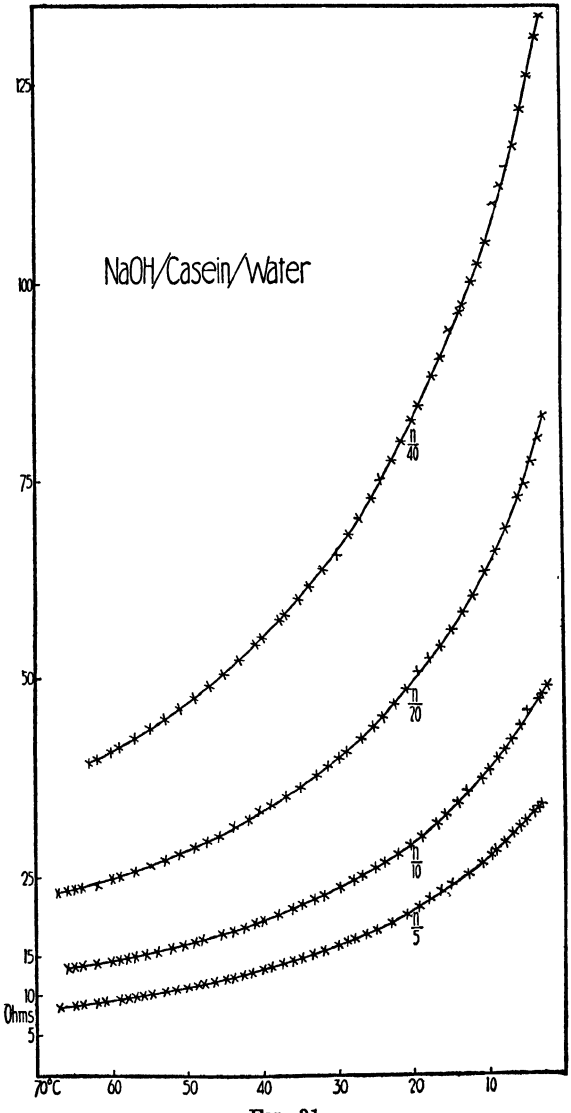
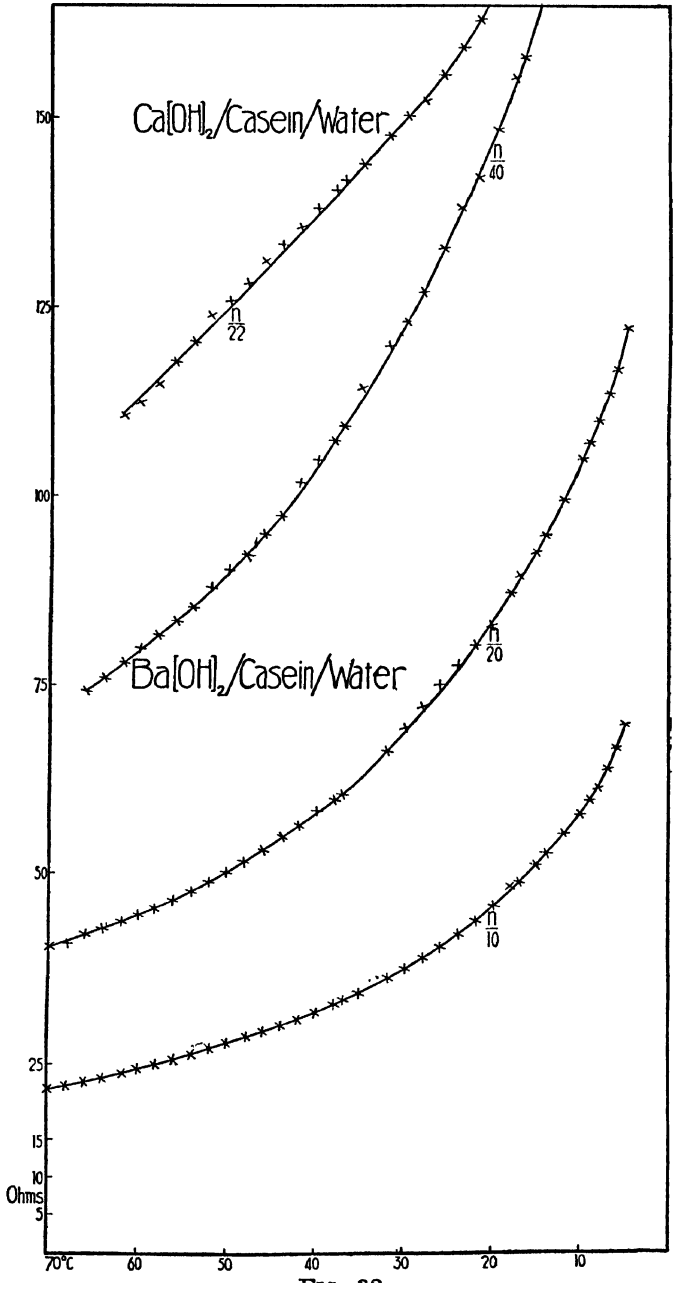

NaOH/Casein/Water
125
100
75
50
25
15
10
5
Ohms
70°C
60
50
40
30
20
10
n/40
n/20
n/10
n/5

FIG. 31


Ca[OH]2/Casein/Water
n/22
n/40
Ba[OH]2/Casein/Water
n/20
n/10
150
125
100
75
50
25
15
10
5
Ohms
70°C
60
50
40
30
20
10

this system obviously increases with dilution. But what is of greater interest to us, the system shows an enormous and abrupt increase in its resistance with falling temperature which is out of all proportion to that registered by any equally concentrated ordinary electrolyte dissolved in water and subjected to similar temperature change. This shows, we think, that these casein salts with water, at the concentrations studied, are not to be thought of as "merely" dilute solution systems. The great increase in electrical resistance in the lower temperature realms is evidence for a change in the type of solution—a change from potassium-caseinate-dissolved-in-water to one of water-dissolved-in-potassium-caseinate and is similar, therefore, to the change

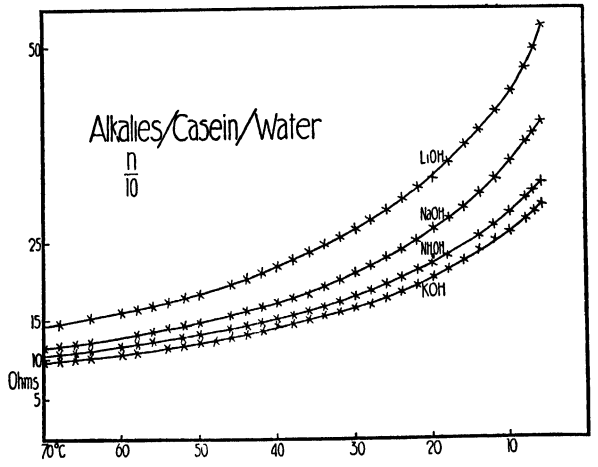


FIG. 33

observed when a solution of phenol or quinolin in water changes to one of inverse type.

Fig. 31 and Table LV illustrate what happens when sodium hydroxid is used instead of potassium hydroxid. The observations made upon potassium caseinate are verified, but comparison of Fig. 30 with Fig. 31 brings out a further interesting fact: at the same concentration, sodium caseinate always registers a higher absolute resistance than potassium caseinate.

This absolutely higher resistance at all temperatures is found to be still further increased when barium or calcium hydroxid take the place of potassium or sodium hydroxid as shown in Fig.

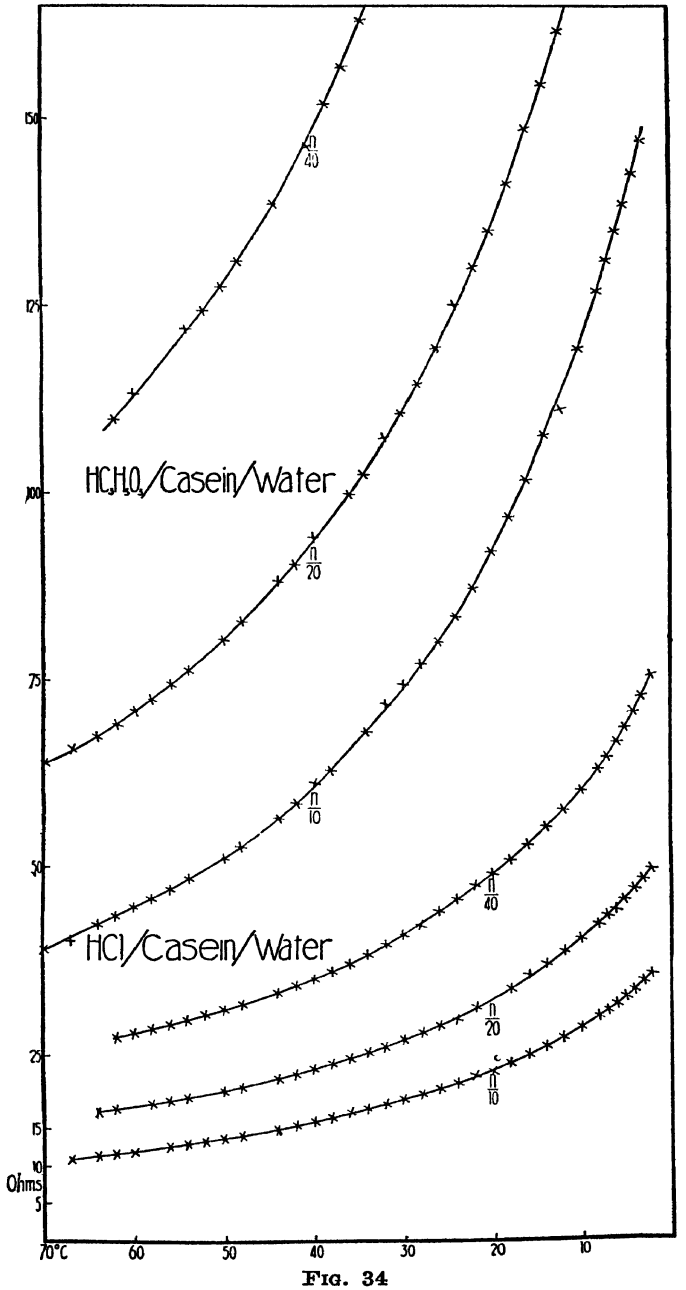

HC2H3O2/Casein/Water
n/40
n/20
n/10
HCl/Casein/Water
n/40
n/20
n/10
150
125
100
75
50
25
15
10
5
Ohms
70°C
60
50
40
30
20
10

FIG. 34

32 and Table LVI. In all these instances the enormous relative increase in electrical resistance with lowering of temperature is again to be observed, this change being even more marked in the alkaline earth caseinates than in those of the alkali metals.

Fig. 33 and Table LVII prove that these differences in the electrical resistance of equally concentrated but different alkali

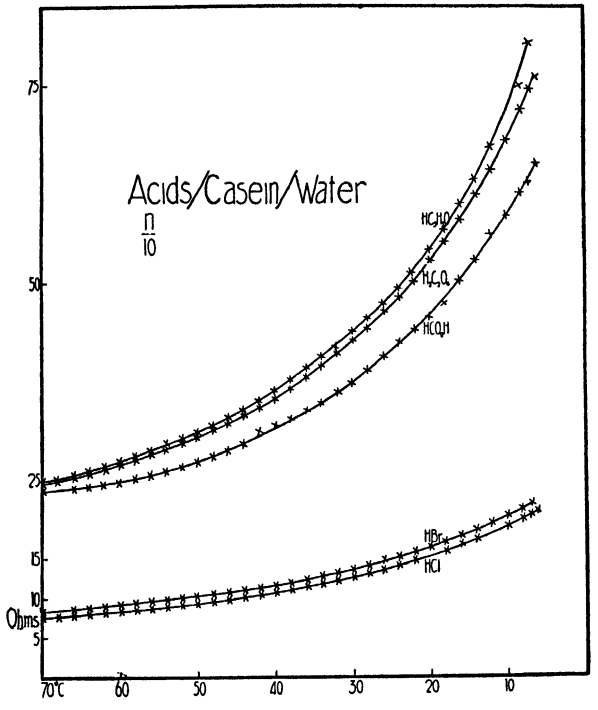


FIG. 35

caseinates are not due to experimental error. The potassium, ammonium, sodium and lithium caseinates were, in this instance, prepared at the same time and in exactly the same fashion. The compounds show an increasing electrical resistance in the order named, the order bearing no relation to the "strength" of the alkalies used or the concentration of hydroxyl ions yielded upon their solution in water, for the ammonium derivative yields a curve which occupies a position in the middle of the series and but little above that of potassium caseinate.

Fig. 34 and Table LVIII which contains the data from which the curves were constructed show the enormous increase in electrical resistance when two different (hydrochloric and lactic) acid casein/water systems are cooled. The curves are self-explanatory. Dilution of an acid casein/water system in each instance increases the electrical resistance. The figure and table

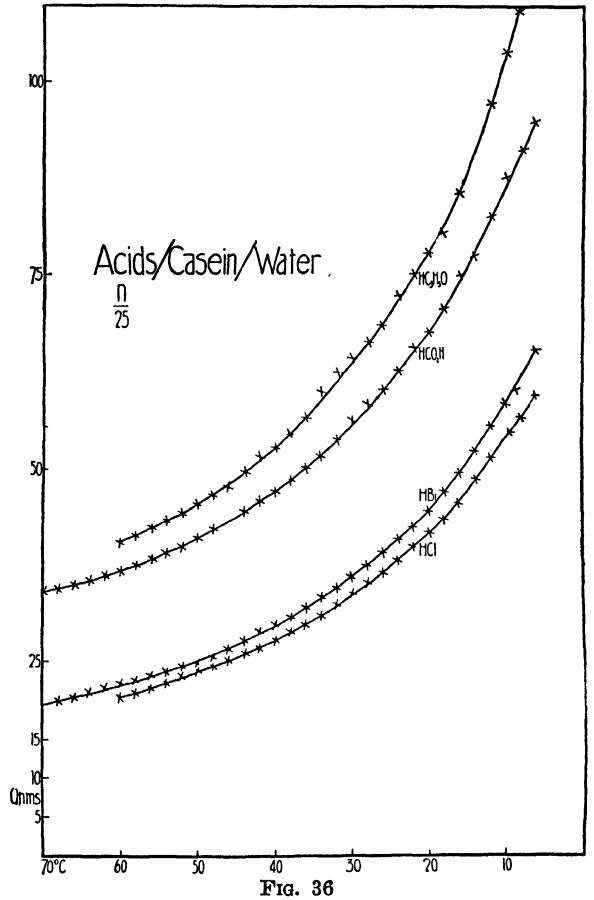


Fig. 36

also show that lactic acid/casein exhibits an enormously higher absolute electrical resistance than a hydrochloric acid/casein of the same "normality."

Figs. 35 and 36, based respectively upon Tables LIX and LX, show besides this increase in electrical resistance upon cooling,

TABLE LIV.—*Electrical resistance in ohms of potassium caseinate/water systems of different concentrations at different temperatures*

° C.	25 grams Casein + 100 cc. 1/5 n KOH	12.5 grams Casein + 100 cc. 1/10 n KOH	6.25 grams Casein + 100 cc. 1/20 n KOH	3.125 grams Casein + 100 cc. 1/40 n KOH
65	6.8			
63	6.9			
61.2	7.1			
59	7.3	11.8		
57	7.5		20.4	
56		12.4	20.6	36.4
55	7.7		20.9	
54		12.5		37.1
52		12.8		37.7
51	8.3		21.9	38.7
50		13.1		39.0
49	8.4		22.6	
48		13.5		
47	8.8		23.0	40.0
45	9.1		24.0	
44		14.3		42.7
43	9.3			43.1
42		14.8		44.1
41	9.6			
40		15.3	25.8	
39	10.0	15.5		45.8
38	10.2			
37.5		15.8		46.8
37			26.8	
36	10.5	16.2		47.9
34	10.8	16.8	28.2	
32.5		17.3	29.1	
31		17.5	29.7	
30	11.6	18.0	30.4	53.6
28	11.9	18.6	31.3	56.0
27			32.4	57.7
26	12.6	19.6	32.7	58.3
25		20.0	33.4	59.1
24	13.2			60.0
23		20.9		61.7
22	13.8		35.5	
21		21.4	36.0	
20	14.7	22.1	37.2	66.1
18.5		22.9		67.2
18	15.2		38.8	
16.5		23.3	39.7	70.2
15	16.3		41.2	72.7
14	17.0	25.1	42.9	74.8
13	17.4	25.7	43.1	76.4
12	18.1	26.4	44.2	78.6
11		27.2	45.1	80.5
10	18.9	28.4	46.5	81.8
9		28.7	47.7	84.2
8		30.0	48.9	86.3
7	20.3	30.4	50.2	88.9
6	21.3	31.5	51.5	91.5
5	21.6	32.9	52.8	94.2
4.5	22.1			
4		34.5	54.2	97.1
3			56.4	99.6
2.3			57.2	102.1
2				103.0
1.5			59.2	

TABLE LV.—*Electrical resistance in ohms of sodium caseinate/water systems of different concentrations at different temperatures*

° C.	25. grams Casein + 100 cc. 1/5 n NaOH	12.5 grams Casein + 100 cc. 1/10 n NaOH	6.25 grams Casein + 100 cc. 1/20 n NaOH	3.125 grams Casein + 100 cc. 1/40 n NaOH
67	8.5		22.9	
66		13.6	23.3	
65	8.8	13.7	23.4	
64	9.0	13.9	23.6	
62	9.2	14.2	23.8	40.1
60		14.3	24.7	40.9
59	9.4	14.4	25.0	41.4
58	9.6	14.6		
57	9.8	14.8	25.6	42.7
55	10.1		26.5	44.0
53	10.5		27.0	45.0
52		16.1		
51			27.8	46.3
50	10.9			
49	11.2	16.7	28.7	47.6
48	11.5	17.1		
47				49.0
46			30.0	
45	12.0			50.4
44	12.1	18.1	31.3	
43	12.5			52.2
42			32.0	
41		19.0		54.6
40	13.3	19.3		55.2
39	13.5		33.9	
38		20.0		57.5
37	13.9		35.0	58.0
36	14.4	20.9		
35	14.6	21.4	36.0	59.9
33.5	15.2	22.0		
32	15.5	22.5		63.6
30	16.1	23.7	40.0	65.4
29	16.7		40.7	
28	17.1	24.5		68.2
27		25.0	42.4	70.2
25.5			43.6	72.8
25	18.0	26.0		
24		26.6	45.0	75.9
22.5		27.5	46.5	77.5
21	20.0		48.4	80.1
19	21.0	30.0	50.8	84.4
18	22.1		52.4	
17		31.7		88.1
16.5	23.2		54.0	
16		32.7		90.4
15	24.0		56.1	94.0
13.5			58.2	96.2
13	25.3	35.7		97.0
12			60.2	100.0
11	26.6	37.1		102.2
10	27.7	38.3	63.3	105.0
9	28.1	40.0	66.0	109.5
8	29.3	40.9		112.0
7	30.5	42.2	68.7	
6	31.3	44.0	72.8	117.2
5	32.0	45.8	74.3	121.8
4	33.0		77.2	126.0
3	34.0	47.6	80.2	131.1
2.5			83.0	133.8
2		48.8		

TABLE LVI.—*Electrical resistance in ohms of barium and calcium caseinate/water systems of different concentrations at different temperatures*

° C.	12.5 grams Casein + 100 cc. 1/10 n $Ba(OH)_2$	6.25 grams Casein + 100 cc. 1/20 n $Ba(OH)_2$	3.125 grams Casein + 100 cc. 1/40 n $Ba(OH)_2$	6.25 grams Casein + 110 cc. 1/22 n $Ca(OH)_2$	3.125 grams Casein + 100 cc. 1/40 n $Ca(OH)_2$
70	21.5	39.6			
68	21.9	40.6			
66	22.4	41.7	74.2		
64	22.8	42.4	75.9		173.9
61.8	23.5	43.5	78.0	110.4	177.4
60	24.0	44.5	79.8	112.2	180.5
58	24.6	45.2	81.5	114.7	184.0
56	25.4	46.5	83.3	117.7	187.0
54	26.1	47.6	85.1	120.3	190.1
52	27.0	49.0	87.8	123.7	194.0
50	27.5	50.1	90.1	125.7	197.7
48	28.5	51.5	92.0	128.0	200.5
46	29.0	53.0	94.8	130.9	204.2
44	29.8	54.9	97.2	133.2	208.8
42	30.5	56.3	101.6	135.5	211.5
40	31.5	58.2	104.6	138.1	214.9
38	32.8	59.7	107.1	140.5	217.6
37	33.3	60.5	109.2	141.8	219.4
35	34.0	62.5	114.4	144.1	223.1
32	36.2	66.0	119.8	147.7	228.7
30	37.3	69.2	123.1	150.6	232.6
28	38.8	72.1	127.0	152.6	241.1
26	40.2	75.0	132.8	156.1	243.6
24	41.8	77.6	138.2	159.8	250.0
22	43.6	80.2	142.3	163.4	258.0
20	45.7	82.8	148.7	166.4	267.0
18	48.3	87.2	155.8	173.2	278.0
17	48.8	89.6	158.5	176.0	282.2
15	51.0	92.4	166.2	181.8	296.4
14	52.6	94.8	172.3	184.8	300.4
12	55.2	99.6	180.3	194.0	318.0
10	57.7	105.1	190.7	202.1	333.8
9	59.7	107.1	193.2	208.8	343.4
8	61.3	110.2	199.6	215.8	360.5
7	63.9	113.9	203.7	225.0	389.5
6	66.6	117.0	212.9	230.7	397.4
5	69.7	122.5	217.2	235.4	405.5

TABLE LVII.—*Electrical resistance in ohms of different alkali caseinate/water systems at different temperatures*

(12.5 grams Casein + 100 cc. 1/10 n Alkali)

° C.	KOH	NH_4OH	NaOH	LiOH
70	9.5		11.4	14.2
68	9.8	10.6	11.7	14.6
66	10.0	10.9	12.0	
64	10.2	11.1	12.2	15.3
60	10.6	11.7		16.2
58	10.9	12.1	13.2	16.5
56		12.4	13.6	17.0
54	11.5		14.1	17.5
52	11.9	12.8	14.4	18.1
50	12.1	13.2	14.6	18.4
46	12.8	13.9	15.7	19.8
44	13.2	14.4	16.2	20.4
42	13.6	14.6	16.9	21.1
40	14.4	15.1	17.5	21.8
38	14.6	15.6	17.9	22.7
36	15.2	16.2	18.4	23.8
34	15.7	16.8	19.5	24.8
32	16.2	17.5	20.3	25.7
30	16.6	18.2	21.2	26.8
28	17.0	18.9	22.1	27.7
26	18.1	19.8	23.1	29.1
24	18.8	20.6	24.0	30.6
22	19.5	21.6	25.1	32.1
20	20.5	22.2	26.8	33.1
18	21.6	23.2	28.1	35.1
16	22.8		29.4	37.5
14	24.0	25.8	31.3	39.2
12	25.3	27.0	33.1	41.7
10	26.3	28.7	35.3	44.3
8	27.8	30.6	37.7	47.2
7	28.7	31.5	38.8	49.8
6	29.8	32.6	40.4	52.8

TABLE LVIII.—*Electrical resistance in ohms of acid caseinate/water systems of different concentrations at different temperatures*

° C.	12.5 grams Casein + 100 cc. 1/10 n HCl	6.25 grams Casein + 100 cc. 1/20 n HCl	3.125 grams Casein + 100 cc. 1/40 n HCl	12.5 grams Casein + 100 cc. 1/10 n Lactic Acid	6.25 grams Casein + 100 cc. 1/20 n Lactic Acid	3.125 grams Casein + 100 cc. 1/40 n Lactic Acid
70				38.8	62.8	
67	10.9			40.0	65.8	
64	11.4	17.0		42.2	67.2	
62	11.5	17.4	27.2	43.4	69.0	109.7
60	11.6		27.8	44.7	70.8	113.4
58		18.2	28.3	45.5	72.2	
56	12.5	18.6	28.8	47.0	74.5	
54	12.8	19.0	29.4	48.5	76.4	121.9
52	13.1		30.2	49.9	78.3	124.2
50	13.6	19.9	30.8	51.0	80.2	127.3
48	14.0	20.4	31.4	52.5	82.6	130.5
44	14.8	21.5	32.9	56.4	88.0	138.5
42	15.3	22.1	34.0	58.4	90.1	
40	15.8	22.9	34.9	61.2	93.7	145.9
38	16.3	23.5	35.8	62.6		151.8
36	17.1	24.4	36.8	65.2	99.6	156.7
34	17.4	25.2	38.1	67.7	102.0	163.1
32	18.1	25.8	39.4	71.5	107.0	169.3
30	18.7	26.8	40.6	74.2	110.3	175.6
28	19.5	27.8	41.8	76.9	114.3	182.1
26	20.1	28.5	43.8	79.8	119.0	
24	20.9	29.2	45.5	83.1	124.9	198.3
22	21.9	31.0	47.4	86.9	129.8	208.2
20	22.3		49.0	91.9	134.7	214.2
18	23.4	33.3	50.7	96.5	141.1	224.6
16	24.6	35.3	52.6	101.5	148.4	
14	25.7	36.8	55.0	107.4	154.5	249.6
12	26.9	38.5	57.4	110.9	161.5	
10	28.1	40.0	60.0	118.9	169.4	273.9
8	29.7	41.9	62.8	126.7	180.7	288.6
7	30.5	43.2	64.2	130.8		293.9
6	31.3	43.9	66.3	134.7	192.6	301.2
5	32.3	45.2	68.3	138.8	199.0	313.0
4	33.1	46.9	70.3	142.5	207.4	325.0
3	34.4	48.2	72.4	146.9	212.8	333.0
2	35.5	49.4	75.4			

TABLE LIX.—*Electrical resistance in ohms of different acid caseinate/water systems at different temperatures*

(12.5 grams Casein + 100 cc. 1/10 n Acid)

° C.	HCl	HBr	Formic	Oxalic	Lactic
70	7.5	8.2	23.6	24.4	
68	7.7			24.8	25.0
66	7.8	8.5	23.8		25.6
64	7.9	8.6	24.0	25.6	26.0
62	8.1	8.8	24.2	26.2	26.6
60	8.3	9.1	24.4	26.8	27.3
58	8.4	9.2	25.2	27.5	27.7
56	8.6	9.4	25.6	28.1	28.5
54	8.7	9.7	26.0	28.5	29.6
52	8.8	9.8	26.4	29.6	30.2
50	9.1	10.0	27.3	30.2	30.9
48	9.3	10.5	27.7	31.3	31.6
46	9.4	10.6	28.5	31.8	32.9
44	9.9	10.7	29.4	33.1	33.6
42	10.2	10.9	31.1	34.2	34.9
40	10.5	11.2	31.8	35.2	36.3
38	10.9	11.7	32.7	36.5	37.5
36	11.3	12.0	33.8	37.9	39.1
34	11.7	12.5	34.7	39.3	40.5
32	12.0	12.9	36.1	40.8	41.5
30	12.3	13.5	37.0	42.5	43.7
28	12.8	13.9	38.6	43.9	45.3
26	13.2	14.6	40.5	46.3	47.1
24	13.7	14.9	42.3	48.1	49.1
22	14.4	15.7	43.9	50.0	51.0
20		16.2	45.4	52.7	54.0
18	15.3	16.6	47.1	54.9	56.6
16	16.5	17.6	50.0	58.0	60.0
14	17.1	18.4	52.7	61.2	63.0
12		19.2	56.0	64.2	67.0
10	18.9	20.3	58.3	67.7	
8	19.6	21.1	61.2	71.8	74.8
7	20.3	21.8	62.6	74.5	80.4
6	20.8		64.9	75.9	

TABLE LX.—*Electrical resistance in ohms of different acid caseinate/water systems at different temperatures*

(12.5 grams Casein + 100 cc. 1/25 n Acid)

° C.	HCl	HBr	Formic	Lactic
60	20.2	22.2	36.5	40.3
58	21.0	22.6	37.5	41.3
56	21.6	23.2	38.4	42.5
54	22.2	23.6	38.9	43.3
52	23.2	24.2	39.7	44.3
50	23.8	24.6	41.0	45.5
48	24.4	25.4	42.4	46.5
46	25.1	26.6	43.8	47.3
44	26.2	27.9	44.5	49.7
42	26.6	29.0	45.8	51.6
40	27.7	29.9	47.1	52.8
38	29.0	30.9	48.6	54.3
36	29.6	32.0	50.0	56.6
34	30.9	33.5	51.6	60.3
32	32.7	34.7	54.0	62.4
30	34.0	35.8	56.5	64.2
28	35.4	37.2	58.6	66.4
26	36.5	39.1	60.3	68.5
24	37.9	40.8	62.7	72.5
22	39.8	42.3	65.8	75.2
20	41.8	44.5	67.7	77.9
18	43.5	47.1	70.8	80.4
16	45.5	49.4	75.2	85.8
14	48.9	52.4	77.6	
12	51.6	55.7	82.9	97.5
10		58.6	88.0	104.2
9.5	54.9			
8.5		60.3		
8	56.8		91.5	109.5
6	59.5	65.5	95.1	115.0

the differences in absolute resistance as determined by the nature of the acid added to the casein. The several caseinates were all prepared in identical fashion. In Fig. 35 an amount of acid was added to the casein which was the equivalent of the alkali in Fig. 33. This amount is generally held to be in excess of the actual quantity that can be bound chemically by this protein.

In Fig. 36 the amount of acid added is that generally held to be just sufficient to neutralize the casein. The curves in this instance lie higher but otherwise show the same general shape and order as in Fig. 35. Lactic, formic, hydrobromic and hydrochloric acids follow each other in the order given when that which registers the highest absolute electrical resistance is mentioned first.

VI. On the Theory of Solvation in Colloids[33]

Having said that in the process of gelation we deal with the change, fundamentally, of a solution of x-in-solvent to one of solvent-in-x, we need to discuss, as far as may be possible, the nature of this second type of solution.

The pure chemist is likely to ask at this point what we mean by the term "solution." The easiest answer is to say that we mean just what he does. But the chemist has never brought us any real definition. He holds, in essence, that a substance has gone into solution when, upon mixture of any two materials, the one disappears so perfectly in the other that the general physical characteristics of the "solvent" are not obviously changed. As a matter of fact, only one of its characteristics has been left thus unchanged and this a very coarsely measured one—ordinary daylight passes through the "solution" in as "homogeneous" a fashion as before. This fact is "explained" by saying that the dissolved substance is dispersed uniformly throughout the solvent, and that the dissolved particles are of molecular size or smaller. Justification for the latter deduction is always found in the fact that there is nothing particulate in the solution of sufficient size to bend the light waves out of their courses. This is the typical "true" solution of the physical chemists, and judged by such a criterion the term may be applied

[33] Martin H. Fischer and Marian O. Hooker: Kolloidchem. Beihefte, *23*, 200 (1926); Kolloid-Zeitschr., *40*, 303 (1926).

to both of the two types of solution which received special discussion earlier, namely those of phenol or quinolin dissolved in water and those of water dissolved in phenol or quinolin.[34]

What we wish to emphasize now, and more particularly for the solutions of the solvent-in-x type, is that this definition is not by itself sufficient to characterize these solutions. What is the nature of the "solutions" formed when for example water "dissolves" in phenol or when water "dissolves" in soap or protein (or, finally, when the hydrophilic colloids of a cell, tissue, or organism "combine" with water to form the water-saturated living mass)? These "solutions" of water-in-x are obviously different from those of x-in-water so familiar to us in the chemical laboratory. We hold that *the water (or other solvent) in all these systems is no longer "free" but combined with the material which is hydrated (solvated).* In most instances, if not in all, we believe also that *this combination is quantitative in character (stoichiometrical), and in this sense "chemical."*

If we look about the chemical laboratory for illustrations of what has been said we think that the analogue of what happens in the case of the *solid* lyophilic colloid systems (like the various sodium soaps of the acetic series with water or alcohol) may be

[34] We confess that it has never been as easy for us as for the physical chemists to be thus sure, on this basis of optical homogeneity, when a material had gone into true "solution." Certain soaps, for example, (like sodium palmitate) with certain alcohols (like benzyl) yield, at higher temperatures, water-clear mixtures of "normal" boiling point and "normal" osmotic pressure (calculated). With lowering of temperature, they become increasingly viscid and then set into solid gels, but *optical homogeneity is maintained throughout the entire set of systems ending in the production of a glass-like body.* The same is true of certain heavy metal soaps (aluminium laurate, myristate, palmitate or stearate, and various cadmium soaps) with a large number of different organic solvents (benzene, toluene, xylene, chloroform, carbon tetrachlorid), as emphasized in the succeeding pages. These systems, even though optically clear, are frankly colloid and must obviously not be compared with the ordinary true solutions of the physical chemists. What we should like to emphasize is that many of the chemists' apparently true solutions (as judged by these optical standards) are really "colloid" and that the explanation of their "peculiarities" is not to be found in further (and violent) modification of the dilute solution laws, but by an application to them of the principle of inverse solution that is being brought out in these pages.

found in the solidification of these various substances into crystals containing various amounts of water or any other "solvent."[35] When, for example, a true solution of sodium stearate in water or alcohol changes to a solid upon cooling, it means that a solid solution of the solvent in the soap has been produced or, differently expressed, that the soap has crystallized out with several molecules of the water or the alcohol. The gelation of a lyophilic colloid system in this case is like the crystallization of any salt with a large fraction of water of crystallization.

But where is the laboratory analogue when dry sodium oleate takes up water to yield an oily liquid, or crystals of phenol take up a limited amount of water to yield an oily solution of water-in-phenol? We think that the analogue may, in these instances, be seen in the liquefaction of (solid and crystalline) sulphur trioxid to sulphuric acid when water is added and in the subsequent behavior of this oily concentrate towards water.

The next pages will look at these systems, so long familiar to the pure chemist, from such a colloid-chemical point of view.[36] Even the ordinary concentrated sulphuric acid of our laboratories is not yet, we think, a solution of H_2SO_4 in water, but one of water in H_2SO_4. The uppermost curve of Fig. 37 and the column marked I of Table LXI show how the electrical resistance of this acid changes with falling temperature. (The electrical resistance was measured in the usual fashion with a widely separated pair of fixed platinized platinum electrodes of the constant 13.4, a Wheatstone bridge arrangement and a telephone.)

The large swing upward in electrical resistance is characteristic of that type of change in solution which occurs when a solution

[35] See page 130.

[36] It need not be pointed out that the measurement of the electrical resistance of sulphuric acid/water systems as detailed here is not new. The values have been redetermined merely to indicate their relationship to the similar values found in phenol/water, soap/water and protein/water systems.

The most extensive measurements of this sort are probably those of R. KNIETSCH: Ber. d. Deut. Chem. Gesellsch. *34*, 4100 (1901). See also the recent studies of R. AUERBACH: Zeitschr. f. physik. Chem. *121*, 337 (1926) who publishes determinations of the molecular weight of water in fuming sulphuric acid, discovering values as high as 90 (instead of 18).

of x-in-water (like phenol in water) changes to one of water-in-x (like water in phenol) and we therefore believe that a similar change occurs in the case of sulphuric acid when cooled. The remaining three curves of Fig. 37 and columns II, III and IV of Table LXI substantiate this. These three curves concern

TABLE LXI.—*Electrical resistance in ohms of sulphuric acid (Sp. Gr. 1.84)/water systems at different temperatures*

° C.	50 cc. H_2SO_4	50 cc. H_2SO_4 + 25 cc. H_2O	50 cc. H_2SO_4 + 50 cc. H_2O	50 cc. H_2SO_4 + 100 cc. H_2O
	I	II	III	IV
65		33.5	18.3	
64		34.2	19.0	11.9
63		34.4	19.1	12.0
62		35.3	19.4	12.1
61		36.0	19.9	12.2
60	52.9	36.4	20.0	12.3
59	53.8	37.5	20.3	12.4
58	55.0	38.1	20.4	12.4
57	55.7	38.5	20.7	12.6
56	57.2	39.0	21.0	12.8
55	57.9	39.7	21.2	13.0
54	58.9	40.6	21.5	13.1
53	60.0	41.6	21.8	13.2
52	61.2	42.6	22.1	13.3
51	62.3	43.2	22.5	13.6
50	63.4	44.3	23.0	14.0
49	65.0	45.3	23.3	14.1
48	65.8	45.9	23.6	14.3
47	66.9	46.6	24.0	14.5
46	68.3	47.2	24.3	14.6
45	69.7	48.3	24.6	14.9
44	71.2	49.4	25.0	15.0
43	72.7	50.6	25.4	15.2
42	74.5	51.2	25.7	15.3
41	75.4	52.4	26.2	15.5
40	77.6	53.1	26.6	15.7
39	79.8	54.3	27.1	15.8
38	81.4	55.5	27.7	16.1
37	83.1	56.7	28.0	16.5
36	85.5	57.9	28.2	16.6
35	87.2	59.7	29.0	16.9
34	90.1	60.7	29.7	17.3
33	90.8	62.3	30.0	17.4
32	94.1	64.4	30.7	17.7
31	95.3	65.5	31.1	18.0
30	98.5	67.5	32.1	18.4
29	99.6	68.3	32.4	18.6
28	102.8	70.9	32.9	18.7
27	104.9	71.8	33.8	19.2

TABLE LXI.—(*Continued*).

° C.	50 cc. H_2SO_4	50 cc. H_2SO_4 + 25 cc. H_2O	50 cc. H_2SO_4 + 50 cc. H_2O	50 cc. H_2SO_4 + 100 cc. H_2O
	I	II	III	IV
26	107.4	74.5	34.2	19.4
25	110.5	76.0	34.9	19.9
24	112.9	78.5	36.0	20.3
23	116.4	79.8	36.6	20.8
22	118.8	82.5	37.5	21.0
21	124.2		38.1	21.3
20	125.2	88.6	39.2	21.9
19	129.3	90.3	39.6	22.4
18	133.6	91.9	40.1	22.5
17	134.7	94.5	41.6	23.5
16		98.0	43.0	23.9
15	145.7	100.8	43.7	24.1
14	147.5	104.4	44.5	24.6
13	151.6	107.0	45.7	25.1
12		110.9		25.7
11	165.3	114.6	48.1	26.3
10	168.8	116.9	49.4	26.6
9	173.9	121.7	50.6	27.0
8	181.7	123.7	51.5	27.7
7	188.1	126.7	52.8	28.2
6	195.5	132.0		28.7
5	205.2	138.6	55.0	29.7
4	210.2	140.9	56.5	30.1
3		146.3	57.7	31.5
2	224.6	151.9	59.7	31.8
1.8	230.9			

themselves with sulphuric acid to which increasing increments of water have been added. They show how upon the addition of water, the electrical resistance of these sulphuric acid/water systems is *reduced*. Diluting the system in other words improves its conductivity, just as in the instance of the systems phenol/water, quinolin/water, soaps/water, etc., when water is added to them.

The long curve of Fig. 38 (drawn from the values recorded in column II of Table LXII) shows the point at which a maximal reduction in electrical resistance is found when concentrated sulphuric acid is diluted with increasing amounts of water. The low point is registered when 200 cc. of water are added to 50 cc. of the acid. Dilutions beyond this point bring with them an *increase* in the electrical resistance according to the familiar laws of the dilute solution chemists. In this left hand, gradually

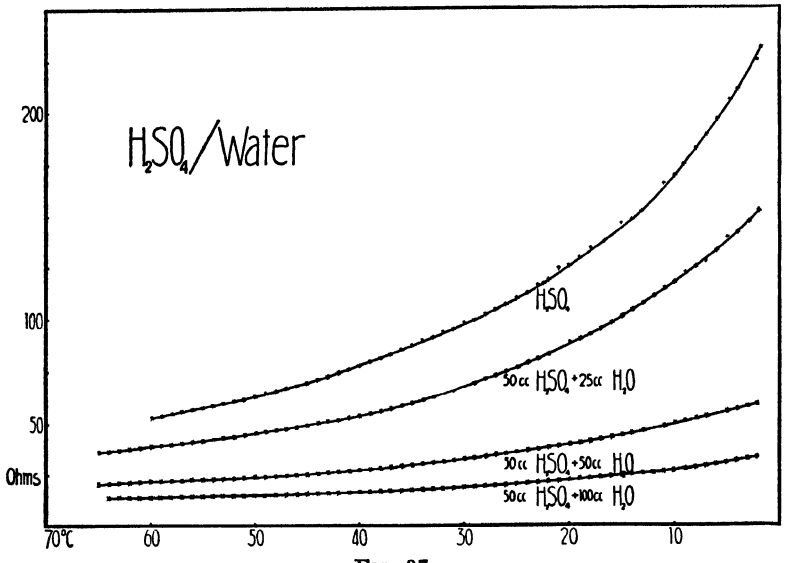


FIG. 37

ascending, portion of the curve, we deal obviously with a solution of sulphuric acid in water; in the right hand long sweep upwards, with what is essentially a solution of water in the sulphuric acid.

This right arm of the curve shows a break near its peak. It has been noted by other authors.[37] It indicates, we think, that

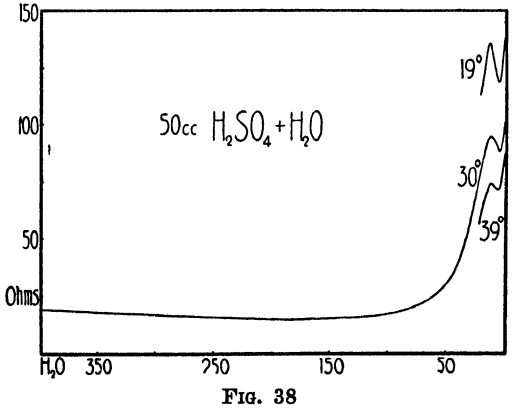


FIG. 38

[37] See, for example, FREDERICK H. GETMAN: Theoretical Chemistry, third edition, 422, New York (1922).

TABLE LXII.—*Electrical resistance in ohms of ordinary sulphuric acid with increasing increments of water at three temperatures*

To 50 cc. of the acid (Sp. Gr. 1.84) are added the following cc. of water	39° C.	30° C.	19° C.
	I	II	III
0	87.7	102.2	135.9
1	78.5		127.3
2	76.2	92.4	122.4
3	73.7		120.5
4	73.1	88.8	119.1
5	72.8		120.6
6	73.1	90.8	124.2
7	73.4		126.0
8	73.7	92.8	
9	74.0		130.5
10	74.6	94.5	131.6
11	75.0		134.5
12	75.0	95.3	136.5
13	73.7		133.8
14	73.4	93.2	
15			131.1
16	70.7	90.4	128.5
17	69.0		121.2
18	67.4	85.5	119.1
19	64.9		115.0
20	57.3	81.9	114.4
22		77.2	
24		69.0	
26		62.6	
30		56.7	
40		38.4	
50		30.3	
60		25.4	
70		23.0	
80		20.8	
90		19.1	
100		18.0	
120		16.6	
140		15.9	
160		15.5	
180		15.4	
200		15.3	
250		16.1	
300		17.0	
350		18.1	
400		19.0	

even concentrated sulphuric acid is not a simple system (namely water "dissolved" in H_2SO_4). We incline to the view that SO_3 is present in the highly concentrated acid at lower temperatures, and that the V shaped break in the ascending arm registers therefore the electrical resistance of a solution of SO_3 in sulphuric acid followed by that of a solution of sulphuric acid in SO_3.

Put another way, this "concentrated" sulphuric acid is a *staggered system* in which (beginning at the extreme right of the curve of Fig. 38) an anhydrid, one or more hydrates, and finally water, succeed each other in mutual solution. *Lowering* of temperature tends to force all these systems in the direction of solvent-dissolved-in-x, which explains, to our mind, the reasons why the first (right hand) portions of these curves, illustrating the electrical resistance of the sulphuric acid, lie highest at 19°, occupy a middle place at 30°, and lie lowest at 39°. (See columns I and III of Table LXII.

If this view is correct, then increasing the concentration of "sulphuric acid" by dissolving SO_3 in it should *increase* the electrical resistance of the system.[38] That this is the case is shown in Fig. 39 and Table LXIII. The upper curve shows the electrical resistance of a fuming sulphuric acid (18.3% SO_3) at various temperatures; the lower reillustrates the electrical resistance of ordinary concentrated sulphuric acid at the same temperatures.

The effects of diluting this *fuming* sulphuric acid with successive increments of water is shown in Fig. 40 and Table LXIV. Excepting that the initial resistances are higher, the curve has the same general shape as that described in Fig. 38.

It does not matter for our purposes what is the chemical theory which is accepted to explain these $SO_3/H_2SO_4/H_2O$ systems, whether, in other words, there is a successive series of hydrates (SO_3, $SO_3 \cdot H_2O$, H_2SO_4, $H_2SO_4 \cdot H_2O$, $H_2SO_4(H_2O)_n$, etc.) or other compounds formed or not. We merely wish to point out that these systems when "concentrated" show properties which are not only obviously different from those of the

[38] See the observation of R. KNIETSCH: Ber. d. Deut. chem. Gesellsch. *34*, 4100 (1901).

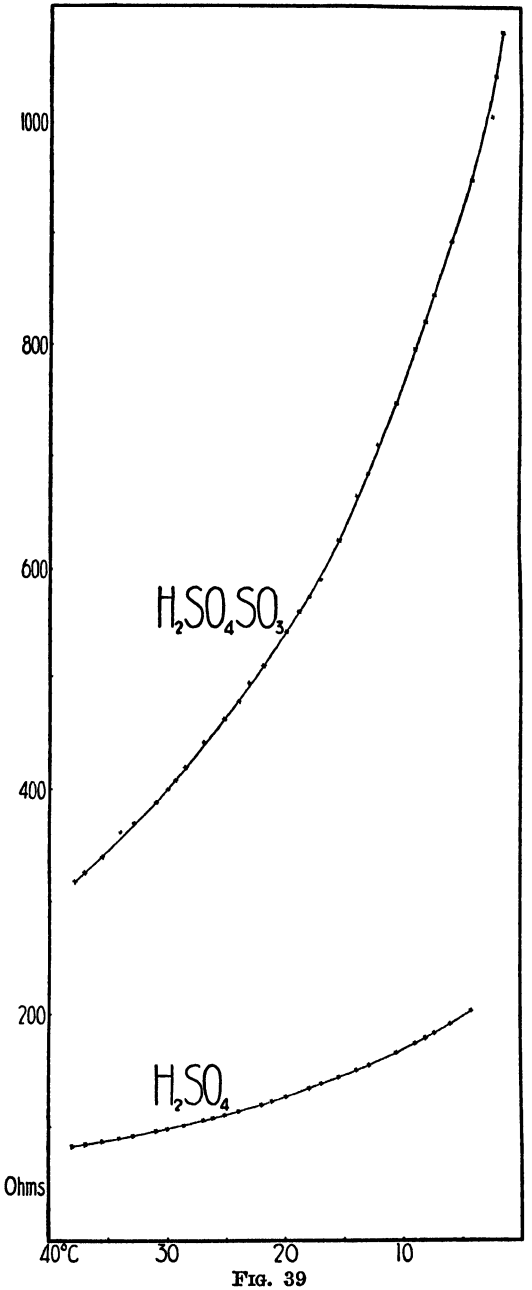

1000
800
600
400
200
Ohms
40°C
30
20
10
$H_2SO_4SO_3$
H_2SO_4

FIG. 39

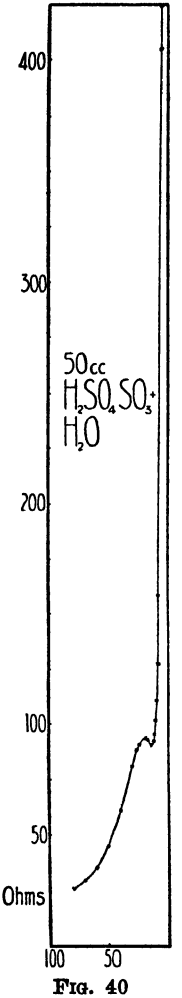

400
300
200
100
50
Ohms
100
50
50cc
$H_2SO_4SO_3$+
H_2O

FIG. 40

ordinary solution of sulphuric acid in water, but that the "hydration" which we observe in hydrophilic colloids (or in protoplasm) is of similar nature.

When SO_3 "dissolves" water to yield (liquid) sulphuric acid, the "hydration" is obviously chemical in nature marking the

TABLE LXIII.—*Electrical resistance in ohms of ordinary sulphuric acid and of fuming sulphuric acid (18.3% SO_3) at different temperatures*

°C.	H_2SO_4	$H_2SO_4SO_3$
38.0	81.5	318.3
37.0	84.0	325.5
35.6	86.0	338.7
34.2	89.3	360.8
33.0	91.5	369.5
31.0	94.5	387.8
30.0	97.0	400.0
29.4		407.7
28.6	100.0	418.6
27.0	105.0	440.5
26.2	107.9	449.4
25.2	110.0	461.8
24.0	113.0	478.0
23.2		495.2
22.0	118.0	509.6
21.2	121.0	521.2
20.0	126.0	549.3
19.0		557.9
18.0	133.5	571.0
17.0	136.5	584.6
15.5	144.0	620.7
14.0	150.0	661.1
13.0	153.8	681.0
12.3		706.4
10.6	165.5	745.0
9.0	174.0	792.0
8.1	178.5	818.0
7.4	183.0	841.8
6.0	190.0	889.1
4.2	203.0	943.0
2.5		1000.0
2.2		1036.0
1.6		1077.0

union of an anhydrid with water. The "solution" is, in other words, "stoichiometrical." In the terminology of colloid chemistry, the original crystals have "dissolved" the water, have "swollen," and yielded a viscid liquid. Put more directly, "solution" in this instance is chemical in nature; and the an-

TABLE LXIV.—*Electrical resistance in ohms of fuming sulphuric acid (18.3% SO_3) with increasing increments of water at 30° C.*

To 50 cc. of acid are added the following cc. of water	Resistance in ohms	To 50 cc. of acid are added the following cc. of water	Resistance in ohms
4	424.7	17	93.9
5	405.5	18	92.7
6	158.6	22	90.3
7	128.2	26	88.4
8	110.8	30	81.1
9	101.6	40	61.2
10	95.5	50	44.7
11	92.7	60	34.9
13	90.0	70	29.4
14	91.9	80	25.4
15	92.3		

TABLE LXV.—*Electrical resistance in ohms of glacial acetic acid with increasing increments of water at 23° C.*

Composition of the system	Resistance in ohms
(1) 50 cc. glacial acetic	664 666
(2) 50 " " " + 10 cc. H_2O	1 890
(3) 50 " " " + 20 " "	465
(4) 50 " " " + 30 " "	253
(5) 50 " " " + 40 " "	167
(6) 50 " " " + 50 " "	129
(7) 50 " " " + 75 " "	91
(8) 50 " " " +100 " "	75
(9) 50 " " " +125 " "	68
(10) 50 " " " +150 " "	64
(11) 50 " " " +200 " "	62
(12) 50 " " " +300 " "	61
(13) 50 " " " +400 " "	63
(14) 50 " " " +500 " "	66
(15) 50 " " " +600 " "	69

hydrid has passed into a new compound, namely the acid. At the same time (and temperature) a solid crystalline mass has given way to a viscid and oily liquid.

Before pushing further this analogy between the nature of solvation in lyophilic colloids and what happens in these better understood chemical systems, we wish to add some observations on another acid anhydrid and its acid, namely acetic acid an-

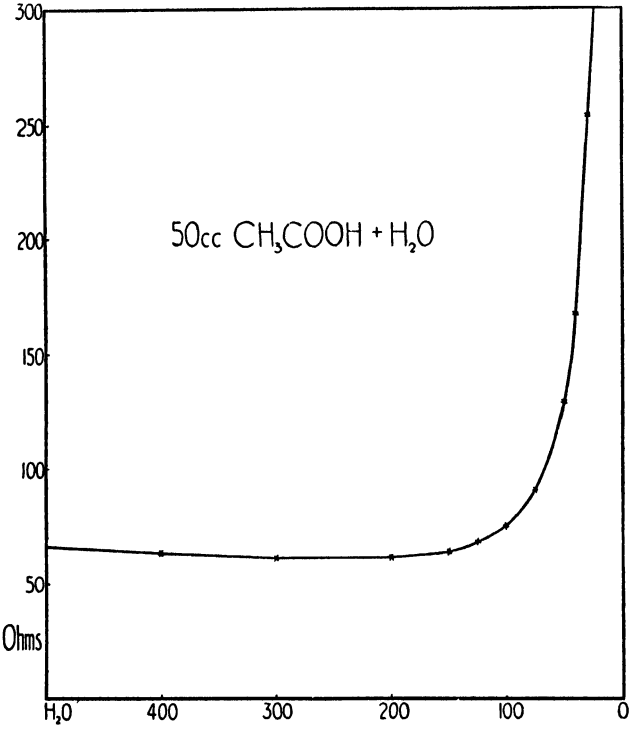


FIG. 41

hydrid and acetic acid. Here, too, the electrical properties of the system show the variations just discussed for sulphuric acid and its anhydrid.

The constant of the electrodes used in these acetic acid experiments was 0.109.

Pure (glacial) acetic acid is a poor conductor of electricity. At 25° C. it registers a resistance of 656,000 ohms. Dilution of the acid *lowers* this resistance so that, at the same temperature,

100 cc. of the acid to which 5 cc. of water have been added shows a resistance of 15,660 ohms; when 10 cc. water are added, 6287 ohms; and with 50 cc. water, 318 ohms. But falling temperature still makes for an unexpectedly great increase in resistance in all these systems. Between 72° and 20° C. the resistance rises (in the form of a rather sharply mounting curve) for these four mixtures, as follows: pure acid, 139,239 to 759,151 ohms; with 5 cc. H_2O, 6712 to 17,809 ohms; with 10 cc. H_2O, 2988 to 6708 ohms; with 50 cc. H_2O, 189 to 355 ohms.

TABLE LXVI.—*Electrical resistance in ohms of glacial acetic acid/acetic anhydrid systems at 23° C.*

	Composition of the system	Resistance in ohms
(1)	50 cc. glacial acetic acid	656 601
(2)	45 " " " " + 5 cc. acetic anhydrid	182 289
(3)	40 " " " " +10 " " "	87 078
(4)	35 " " " " +15 " " "	41 278
(5)	30 " " " " +20 " " "	31 490
(6)	25 " " " " +25 " " "	23 896
(7)	20 " " " " +30 " " "	19 237
(8)	15 " " " " +35 " " "	19 496
(9)	10 " " " " +40 " " "	14 629
(10)	5 " " " " +45 " " "	12 073
(11)	50 " " "	29 367

Fig. 41 and Table LXV show the effects of increasing increments of water upon the electrical resistance of glacial acetic acid. The general form duplicates the curve for sulphuric acid (Fig. 38) when this is diluted with water. The lowest electrical resistance is found when some 300 cc. of water are added to 50 cc. of the glacial acetic acid. To the left of this point, the electrical resistance rises with increasing dilution (of the system acetic acid in water); but it rises much faster and higher to the right of this point (as proof that the water is here dissolved in the acetic acid) pure acetic acid registering the highest electrical resistance of all.

In analogy to what happens when SO_3 is added to sulphuric acid, we may add acetic anhydrid to glacial acetic acid. The effect is shown in the lower curve of Fig. 42 and Table LXVI,

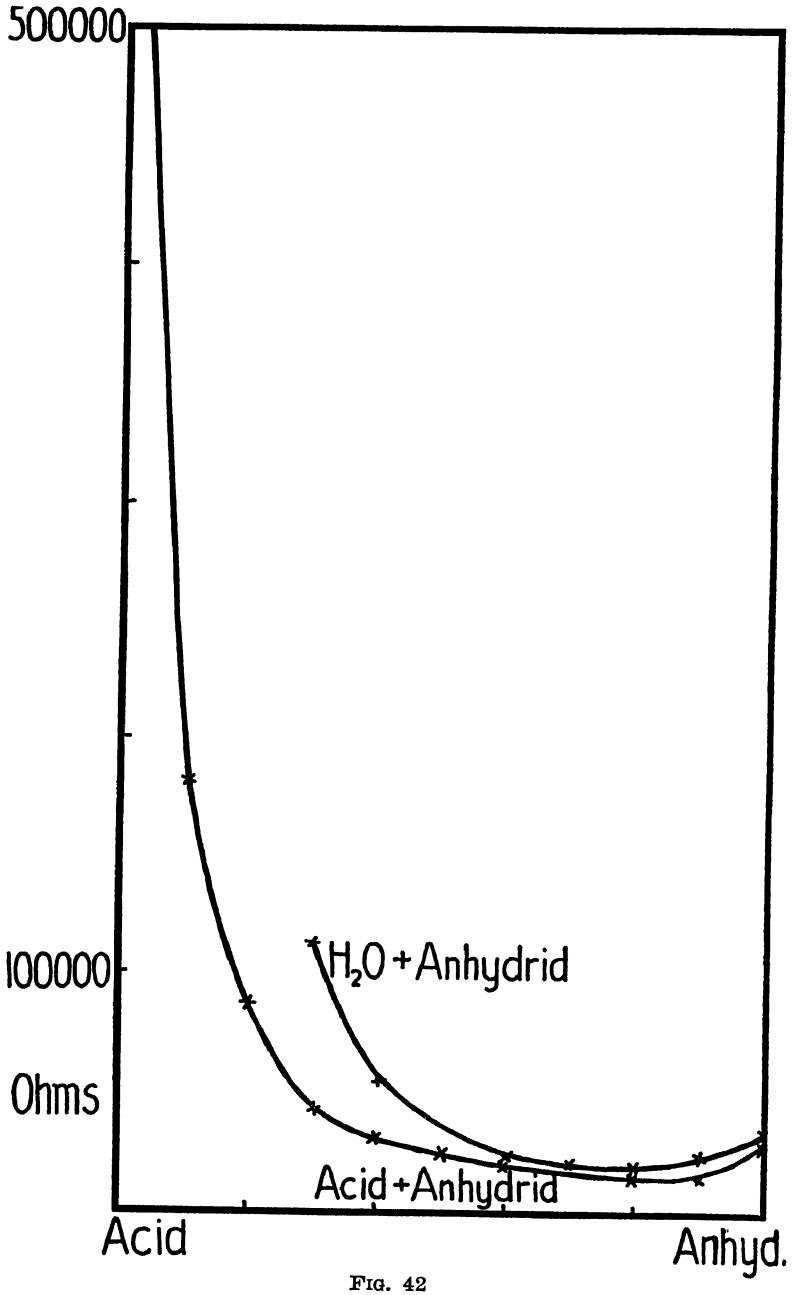


FIG. 42

and duplicates what was previously described in the instance of sulphuric acid. The addition of acetic anhydrid at first *lowers* the electrical resistance of glacial acetic acid, to be followed later by a slight swing upward as the pure anhydrid is approached. We hold that this, too, is indicative of a change in type of solution (from one of the anhydrid in the acid to one of the acid in the anhydrid).

The upper curve of Fig. 42 and Table LXVII show the effects of increasing increments of water upon acetic anhydrid until an amount has been added to yield (after standing for two days at room temperature) glacial acetic acid. Reading the curve from right (the pure anhydrid) to left (the produced glacial acetic

TABLE LXVII.—*Electrical resistance in ohms of acetic anhydrid with increasing increments of water at 24° C.*

Composition of the system	Resistance in ohms
(1) 51 gms. acetic anhydrid	28 333
(2) 51 " " " + 1 gm. H_2O	23 089
(3) 51 " " " + 2 " "	17 218
(4) 51 " " " + 3 " "	19 675
(5) 51 " " " + 4 " "	21 178
(6) 51 " " " + 5 " "	35 868
(7) 51 " " " + 6 " "	54 510
(8) 51 " " " + 7 " "	113 737

acid) it is obvious that the same changes in electrical resistance are registered as though different proportions of the pure anhydrid had been mixed with glacial acetic acid from the start.[39]

[39] These analogies between the properties of concentrated sulphuric acid/water systems and concentrated acetic acid/water systems and those of solvated colloids go beyond those touched upon in these paragraphs. Both acids are viscid when concentrated. When exposed to an atmosphere which contains water vapor, they take up water; in other words, they "swell," as first pointed out by J. R. KATZ: Kolloidchem. Beih., *9*, 1 (1917). This taking up of water is moreover associated with the liberation of heat. Similarly, gelatin and other protein colloids, when cast into water, swell and give off heat (see page 128). Neither does concentrated sulphuric acid nor acetic anhydrid behave like an ordinary acid toward indicators (see page 113). And this "abnormal" behavior towards indicators is also paralleled by a similar behavior on the part of various hydrated (solvated) colloids (see pages 118 and 225).

VII. Further Differences between Solutions of x in a Solvent and Those of the Solvent in x

The preceding pages have emphasized chiefly the large electrical differences that may be observed when a solution of x in the solvent passes into one of the solvent in x; and how various colloid systems, when they gel, exhibit a similar change. We shall now look at some other characteristics of these two types of solution to see if they also cannot be rediscovered in lyophilic colloid systems whenever they pass through the gelation zone.

1. *The solvent properties for any third substance of a solution of x-in-a are totally different from those of a solution of a-in-x,*

When a third substance is added to a phenol/water system, the following may be noted. Hydrated phenol is a better solvent for Nile-blue sulphate, neutral red, methyl red, methyl violet, methyl green, erythrosin B and many other dyes than is the phenolated water in equilibrium with it; the phenol phase will deplete the water phase almost completely of color within a few hours. Eosin and iodin enter the phenol phase more slowly, and relatively more of these materials is left behind in the aqueous phase. The ordinary salts are taken from the water phase not only most slowly but in very small amounts. When colored salts are chosen, the differences in distribution between the two phases make a striking contrast. Ferric chlorid, cupric acetate, cerium sulphate (or their hydrolytic products) enter the phenol phase with increasing difficulty, while chromic chlorid, chromic sulphate and the chlorids of cobalt and nickel seem to remain entirely in the aqueous phase. Of "colloid" substances, infusorial earth concentrates in the aqueous phase while bone black concentrates in the phenol.

Much the same general differences may be observed when the solvent properties of quinolined water are compared with those of hydrated quinolin. Nile-blue sulphate, neutral red, methyl violet, methyl green and iodin pass from the aqueous phase into the quinolin phase to concentrate there. Eosin, methylene blue and methyl red color both phases about equally, while different inorganic salts, like nickel chlorid, chromium chlorid, copper acetate and ferric chlorid remain, so far as color appearances go, entirely in the aqueous phase.

What is generally said of such experiments as these is that they illustrate merely the distribution law of BERTHELOT and JUNGFLEISCH—in other words, the better "solvent" properties of one material as compared with another for a third substance. We concur in this view, but *we insist that a necessary corollary be accepted with it.* In the illustrations here discussed, *both phases contain the same solvents, namely, water with phenol or quinolin, but the solvent properties of the two phases are totally different depending upon the fact—to use our terminology—of whether the water is the solvent for x, or x is the solvent for the water.*

What this means for the solvent properties of hydrated colloids as compared with the solvent properties of the ordinary "dilute aqueous solution" and so for our point of view in biology and physiology, for example, will be made more clear later.

2. *A solution of x-in-a behaves entirely differently toward an indicator than one of a-in-x.*

Neither phenol nor quinolin has sufficient "acidic" or "basic" character to make this difference easily demonstrable, but sulphuric acid/water, acetic anhydrid/water, any soap/water or any protein/water system—all of them systems which, so far as we know, have never been considered from any other point of view but as solutions of *x*-in-*a*—show this difference in striking fashion.

When methyl red, for example, is added to the ordinary concentrated sulphuric acid of the laboratory, it turns bright yellow, indicating, in other words, that this material is violently "alkaline." Upon the addition of water (about one third), the color changes to orange (the mixture becomes "neutral"), and from this point on, increasing increments of water turn the system increasingly red (or in indicator phraseology, increasingly "acid"). Instead of the ordinary physico-chemical interpretation of what has happened, we hold this experiment to prove that concentrated sulphuric acid is not a concentrated solution of this material in water but one of inverse type, namely, one of the water in the acid. As such, it is a solvent for the methyl red different from water and one which, for reasons unknown, gives it a yellow color. The addition of increasing fractions of water gradually changes the total system to one of the ordinary type

of solution, and as this happens, the characteristic "acid" properties and the red color of this indicator make their appearance.

What has been said of the behavior of methyl red is duplicated by other indicators that have been studied, as paranitrophenol (yellow to colorless) and dibromphenolsulphonphthalein (purplish red to yellow).

It has been pointed out elsewhere in this volume that the addition of the first increments of water to concentrated sulphuric acid (yielding in our terminology a solution of the water in the sulphuric acid) is best conceived of as a union of the water with the acid. Put yet another way, an anhydrid unites with water. In the case of sulphuric acid, this union takes place, as it were, instantaneously. We can better follow the process of union if some other anhydrid is taken in which such union takes place more slowly. Acetic anhydrid, when methyl red is added to it, yields an orange color (indicating that this "pure acid" is "neutral"). If water is poured upon the anhydrid, the watery phase at once turns bright red. In other words, a very little of the anhydrid "dissolved" in the water yields a strongly acid system. But the anhydrid which remains behind as a separate phase and which only slowly "dissolves" the supernatant water keeps its neutral reaction for an hour or more. During this time it will not mix with the water. Gradually, however, it too turns red; and now when the system is shaken, it will mix with what was formerly the aqueous phase, to yield a single, uniformly red liquid.

We have described previously[40] how pure, chemically produced neutral soaps behave similarly. A 20 percent mixture of potassium oleate with water, for example, leaves phenolphthalein colorless. If now water is slowly layered upon this mixture, the water becomes increasingly red with increasing dilution of the soap. Between the bottom and the top of such a tube we may read off any C_H or pH we choose.

In the terminology of the physical chemists, we have in this instance begun with a "concentrated" solution of an electrolyte in water—a solution in which hydrolysis and ionization were "suppressed"—and through dilution with water we invited in-

[40] MARTIN H. FISCHER and MARIAN O. HOOKER: Chemical Engineer, *27*, 271 (1919); Soaps and Proteins, 77, New York (1921).

creasing hydrolysis. Potassium hydroxid being stronger as an alkali that oleic acid is as an acid, we thus obtained an overplus of hydroxyl ions yielding us the red color with phenolphthalein. We do not, of course, deny that some of these things happen, but what we should like to point out is that *the first and primary change in this experiment has been missed. This is the conversion, through dilution, of what was originally a solution of the water in the soap to one of the soap in the water.* The indicator serves to show us that these two types of solution are different.

What needs emphasis is that we have been using indicator methods derived from and perhaps applicable to the study of solutions of the type, electrolyte dissolved in water, upon solutions of the opposite type (the most varied chemical mixtures of industry and such biological systems as blood, lymph, or the body tissues) as though these were solutions of the same construction. Obviously there is danger in such thinking.

In the case of potassium oleate with water, the solution of water in the soap passes smoothly and quickly into the solution of soap in the water. The described indicator changes may therefore be even more strikingly observed if, instead of a liquid soap/water system, a hydrated solid soap/water system is employed. Any cake of toilet soap may be used, though the experiment may be made more scientific, quantitative and expensive by utilizing any chemically neutral solid white soap of the acetic series. Even the commercial soaps contain a considerable fraction of water. If some phenolphthalein is poured over the surface of such a cake, no color change takes place. But as soon as distilled water is sprayed upon it, the cake drips red.

The combinations formed between alkalies of various sorts and the proteins behave similarly. A heavily hydrated basic proteinate (like hydrated casein united with any amount of any alkali that does not exceed what may be deemed its neutralization equivalent) gives no color to phenolphthalein, provided the amount of water in the total system is not too large. But mere dilution of such a system (as in the case of the soaps) will yield any depth of red desired. Mere heating of such an alkali protein/water system brings about the same change (because by this method the total system suffers a shift from a solution of the water in the proteinate to one of the proteinate in the water).

Such *p*H values may be shifted to the other side of the ledger by employing an acid proteinate instead of a basic one. Casein (or any other protein) with any acid we may care to tie to it is also "neutral" if too much water is not present in the total system. Increasing increments of water added to such a proteinate turn it increasingly acid. And this shift toward the acid side may also be accomplished by merely warming the mixture, with a return to the neutral upon cooling.

It is such facts as these that have made us hesitate to accept as final the neutralization figures for the proteins that have been published from time to time by different authors for, obviously, the element of mere concentration of the *water* in the systems upon which they worked (and ignored by them) has everything to do with the place at which a "neutral" point may be discovered.

3. *The optical properties of a solution of x-in-a are different from those of a solution of a-in-x.*

In the case of most lyophilic colloid systems, this difference is so great that it is used as proof of the existence of a colloid system. A hot solution of a light metal soap in water, for example, is as clear as hot water itself. But as the mixture is cooled, it becomes opalescent, a proof, in other words, that an internal rearrangement has taken place which no longer allows ordinary light to pass through it as uninterruptedly as before. A similar change may of course be observed in all other types of colloid systems produced by such "condensation" methods. This interruption to the passage of mixed light which manifests itself first in the realm of the shorter waves, namely the violet, may of course become so marked as to take in all the wave lengths of the visible spectrum. From an optically clear solution of *x*-in-*a* (a hot solution of sodium stearate in water or alcohol, for example) we may therefore derive an opaque solution of *a*-in-*x* (a cold white "cake" of the water or alcohol in the soap).

We are, however, familiar with instances in pure colloid chemistry in which such change in type of solution is associated with *no* such coarse or obvious change in light transmission. Thus various light metal soaps (like sodium palmitate) with certain alcohols (like benzyl alcohol or the glycols) yield systems which at higher temperatures are mobile and water-clear mixtures, but

which at lower temperatures change into solid *glass-like* bodies.[41] They constitute, in general, the so-called transparent toilet soaps. In the succeeding pages[42] are described systems composed of heavier metal soaps with various hydrocarbons which also gel into such optically clear systems. The list might be extended by calling attention to various silicate/water systems and certain protein/water or protein/alcohol systems.

TABLE LXVIII.—*Effect of increasing increments of water upon the refractive index of ordinary sulphuric acid (Sp. Gr. 1.84) at 25° C.*

Number of cc. of water added to 50 cc. of acid	Refractive index	Number of cc. of water added to 50 cc. of acid	Refractive index
0	1.4272	200	692
4	330	250	635
8	358	300	611
12	362	350	569
16	340	400	539
20	316	450	515
25	280	500	510
50	095	750	459
100	1,3880	1000	430
150	768		

In order to strengthen further this analogy between the lyophilic colloids and the solutions which we have designated as of inverse type (but which also remain optically clear as the transition is made) we introduce the following observations on sulphuric acid/water systems and sulphuric acid/fuming sulphuric acid systems, only instead of contenting ourselves with the observation merely of the transmission of mixed daylight (which shows no appreciable change) we measure the refractive index.

In the large rectangle of Fig. 43 (the experimental data are given in Table LXVIII) are shown the effects upon the refractive index of ordinary concentrated sulphuric acid when this is diluted with water. The right edge of this rectangle marks the

[41] MARTIN H. FISCHER and MARIAN O. HOOKER: Soaps and Proteins, 49, New York (1921).

[42] See page 168.

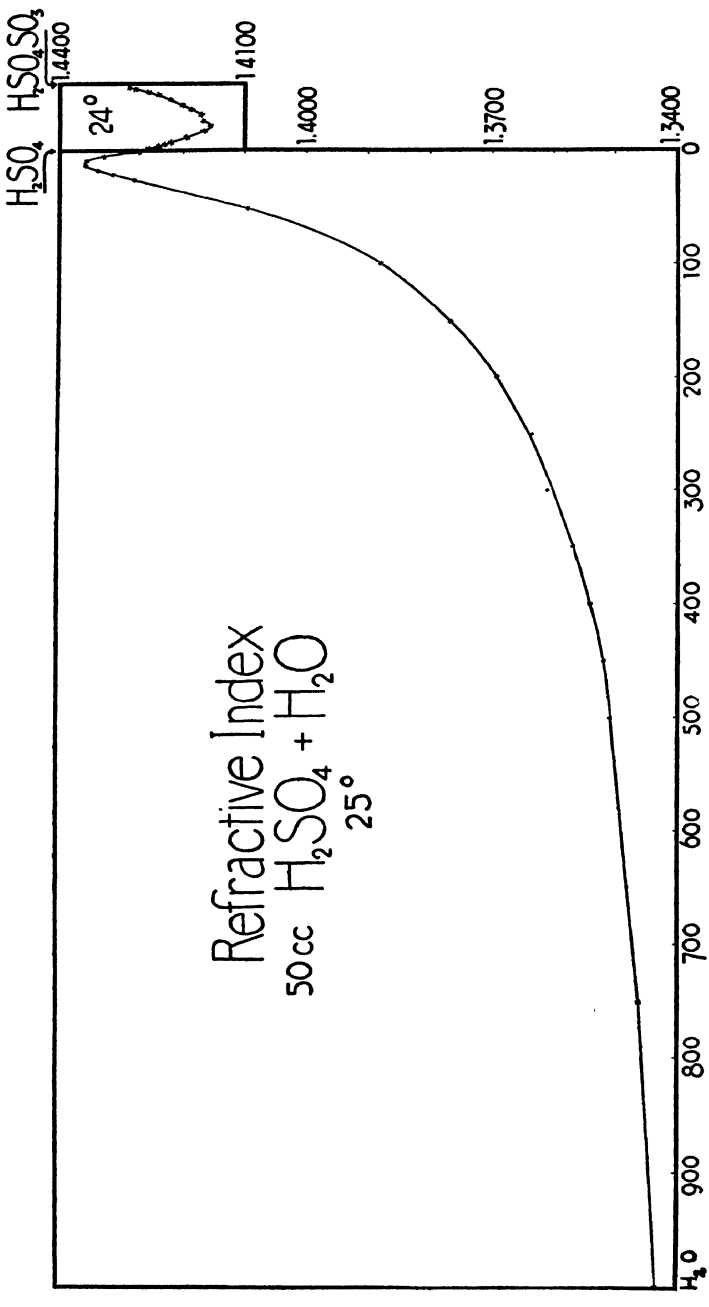

H2SO4
H2SO4SO3
1.4400
1.4100
24°
1.4000
1.3700
1.3400
0
100
200
300
400
500
600
700
800
900
H2O
Refractive Index
50cc H2SO4 + H2O
25°

FIG. 43

refractive index of the pure acid. It will be noted that the addition of the first increments of water increases this value (the curve rises as read to the left) until a high point is reached, beyond which there is an abrupt fall. The curve of this abrupt fall begins to flatten, however, when about 200 cc. of water have been added to 50 cc. of the concentrated sulphuric acid. These breaks in the total curve (*which are practically identical in position with the breaks observable when the electrical resistance of*

TABLE LXIX.—*Effect upon the refractive index of mixing fuming sulphuric acid (31.9% SO_3) with ordinary sulphuric acid (Sp. Gr. 1.84) at 24° C.*

Composition of the system	Refractive index
25 cc. fuming sulphuric acid	1,4286
25 " " " " + 1 cc. ordinary sulphuric acid	280
25 " " " " + 2 " " " "	278
25 " " " " + 3 " " " "	255
25 " " " " + 4 " " " "	252
25 " " " " + 5 " " " "	240
25 " " " " +10 " " " "	220
25 " " " " +15 " " "	200
25 " " " " +20 " " " "	189
25 " " " " +25 " " " "	170
20 " " " " +25 " " " "	158
15 " " " " +25 " " " "	168
10 " " " " +25 " " " "	196
5 " " " " +25 " " " "	222
4 " " " " +25 " " " "	229
3 " " " " +25 " " " "	230
2 " " " " +25 " " " "	240
1 " " " " +25 " " " "	248
25 " " " "	256

these systems is measured[43]) are proofs, to our minds, that something besides mere dilution of the sulphuric acid in the water has taken place. We believe that in the first left-hand portion of the total curve we are measuring the index of refraction of a solution of sulphuric acid in water; that the sharp middle ascent measures the index of what is essentially a solution of the water in the sulphuric acid, and that the break downwards at the ex-

[43] See page 102.

treme right of the curve is due to the presence of SO_3 dissolved in the sulphuric acid.

A test of the last statement is offered in the small rectangle of Fig. 43 and in Table LXIX. In this instance, ordinary sulphuric acid has had increasing increments of fuming sulphuric acid added to it, to end with the pure fuming acid. The left-hand first portion of this curve, it will be noted, is continuous with the right-hand descending arm of the curve in the large rectangle until a low point is reached, after which it rises. We hold that we are measuring successively here a solution of SO_3 in sulphuric acid followed by one of the sulphuric acid in SO_3.

VIII. On the Cooling Curves of Gelling Colloids[44]

In proof of the theory that lyophilic colloids in the process of gelation pass from what is originally a solution of the colloid in the solvent to one which is, in the end, a solution of the solvent in the colloid, we have thus far directed attention to the following differences observable in the transition realm in an otherwise fixed system: (a) a break in electrical resistance; (b) a break in solvent powers for a third substance; (c) a break in behavior toward an indicator; (d) a break in refractive index. There occurs also (e) a change in thermal properties,[45] which is now to be considered.

In discussing the sudden and large increase in electrical resistance shown by any soap/water system when, on cooling, this changes from a sol to a gel, it was noted that in this region the temperature of the cooling colloid system "steadies or actually increases"[46] for a time. If such curves as those given in Figs. 22 and 25 are examined carefully, it will be noted that the recorded temperatures, at the breaks in the curves, after falling to a given low point, rise for a time (the observed temperatures lie to the

[44] Martin H. Fischer: Kolloid-Zeitschr. *46*, 359 (1928).

[45] Martin H. Fischer: Kolloid-Zeitschr., *34*, 145 (1924); 1925 Mayo Foundation Lectures, 89, Philadelphia (1927).

[46] Martin H. Fischer: Science, *57*, 724 (1923); Kolloid-Zeitschr., *33*, 131 (1923); ibid., *33*, 208 (1923); ibid., *34*, 97 (1924); ibid., *34*, 139 (1924); ibid., *35*, 138 (1924); Kolloidchem. Beih., *23*, 200 (1926); Kolloid-Zeitschr., *40*, 303 (1926); the preceding sections.

left of the breaks in the curves). Such observations indicate that in the process of gelling, a lyophilic colloid sets heat free. The following paragraphs give some further details regarding this exothermic phenomenon.

The experiments concern themselves with the cooling rates of gelling colloids. They were all carried out in identical fashion by recording the fall in temperature of a heated and given mass (50 cc.) of various lyophilic colloids contained in a standard container (a test-tube 2.7 cm. in diameter) when plunged into a cold water thermostat of constant temperature (6° C.) and of large capacity. Time was recorded with a split seconds watch.

In Fig. 44 (based upon the data contained in Table LXX) is shown graphically how the temperature of four different half molar sodium soaps of the acetic series falls under such circumstances. *The fact of interest is that a break occurs in each of the curves in that temperature zone at which the previously hot and clear solution of the soap in water changes to the cooler, opalescent or white solution of the water in the soap.* These breaks for sodium laurate, myristate, palmitate and stearate occur at successively higher temperature levels corresponding with the fact that the solubilities of these soaps *in* water decrease in the order given, while their capacity for *taking up* water increases in the same order.

In Fig. 45 (plotted from the data contained in Table LXXI) the same fact is brought out for three 1/8 molar sodium soaps of the acetic series with absolute alcohol. These systems were chosen because their components show the properties of mutual solubility so necessary for this theory of the lyophilic colloid but very little of those electrical properties still so largely emphasized by many workers as of dominant importance for the explanation of the stability of colloids. Beyond directing attention to the breaks, again readily apparent in each curve when gelation of the system takes place, the figure and data are self-explanatory.

These liberations of heat stand out more clearly when, instead of the temperature course, the temperature *change* per unit of time, in other words, the values $\Delta t/\Delta Z$ are calculated and plotted. This has been done by WOLFGANG OSTWALD. The calcu-

TABLE LXX.—*Cooling rate of ½ molar sodium soap/water systems*

Minutes after immersion in a water bath at 6°	Sodium stearate		Sodium palmitate		Sodium myristate		Sodium laurate	
	t	Δ*t*	*t*	Δ*t*	*t*	Δ*t*	*t*	Δ*t*
0								
15					87			
30	86		76		81	6		
45	81	5	72.5	3.5	71	10		
1	73.5	7.5	66	6.5	62	9		
15	66	7.5	62	4		6	55	
30	60	6	57	5	50	6		
45	56.5	3.5	53.5	3.5	44.5	5.5		
2	52.5	4.5	51	2.5	39.5	5	30	
15	50.5	2	48.5	2.5	35.5	4		
30	49	1.5	48	0.5	32	3.5		
45	48	1	47	1		1		
3	46.5	1.5	45	2	30	1	21.5	
15	45	1.5	43	2	30	0	20	
30	43	2	40.5	2.5	32	2		
45	40.5	2.5	38	2.5	31.5	0.5	17.5	
4	38.5	2	36.5	1.5	29	2.5	16	
15		2	33	3.5	28.5	0.5		
30	34.5	2		1.25	27	1.5		
45	32	2.5	30.5	1.25		0.95		
5	30	2	29.5	1	25.1	0.95	13.5	
15		1.25	28	1.5	24	1.1		0.5
30	27.5	1.25	26	2	23	1		0.5
45	26	1.5	25.2	0.8	22	1		0.5
6			24	1.2	21	1	11.5	0.5
15						0.75		0.25
30					19.5	0.75	11	0.25
45						0.75		0.125
7					18	0.75		0.125
15						0.7		0.125
30					16.6	0.7	11.5	0.125
45					16.2	0.4		0.
8					15.6	0.6	11.5	0.
15						0.37		0.15
30						0.37	11.2	0.15
45					14.5	0.37		0.35
9					14	0.5	10.5	0.35
15						0.25		0.125
30					13.5	0.25		0.125
45								0.125
10							10	0.125
15								0.25
30							9.5	0.25
45								0.15
11							9.2	0.15
12							8.7	0.5
13							8	0.7
14							7.5	0.5

TABLE LXXI.—*Cooling rate of $\frac{1}{8}$ molar sodium soap/alcohol systems*

Minutes after immersion in a water bath at 6°	Sodium palmitate*		Sodium myristate*		Sodium laurate	
	t	Δ*t*	*t*	Δ*t*	*t*	Δ*t*
0	73					
15	66	7	74		62	
30	62	4		3	60	2
45	60	2	68	3	56.5	3.5
1	59	1	65.5	2.5	53	3.5
15	58	1		3.75	51	2
30	57	1	58	3.75	50	1
45	55	2	56	2	49	1
2	52.5	2.5	57	1	47.5	1.5
15	51	1.5	56.5	0.5	46.2	1.3
30	48.5	2.5	56	0.5	44.5	1.7
45	46.7	1.8	55	1	43.5	1
3	45.2	1.5	54.5	0.5	41.5	2
15		1.35	53.2	1.3	40.5	1
30	42.5	1.35	52.2	1	39	1.5
45	41.1	1.4	50.5	1.7	37.6	1.4
4	39.5	1.6	49	1.5	36.5	1.1
15	38.5	1	47.5	1.5		1.45
30	37.5	1	46.5	1	33.6	1.45
45	36.2	1.3		1.5		1.15
5	35.1	1.1	43.5	1.5	31.3	1.15
15		1	42.1	1.4	30.2	1.1
30	33.1	1	41	1.1	29	1.2
45		1	39.5	1.5	28	1
6	31.1	1	38.5	1	27	1
15					26	1
30						1
45					24	1
7					23.2	0.8
15					22.5	0.7
30					21.5	1
45						0.65
8					20.2	0.65
15					19.2	1
30					18.8	0.4
45					18.1	0.7
9					17.7	0.4

* The soap will not dissolve entirely in the alcohol at its boiling point.

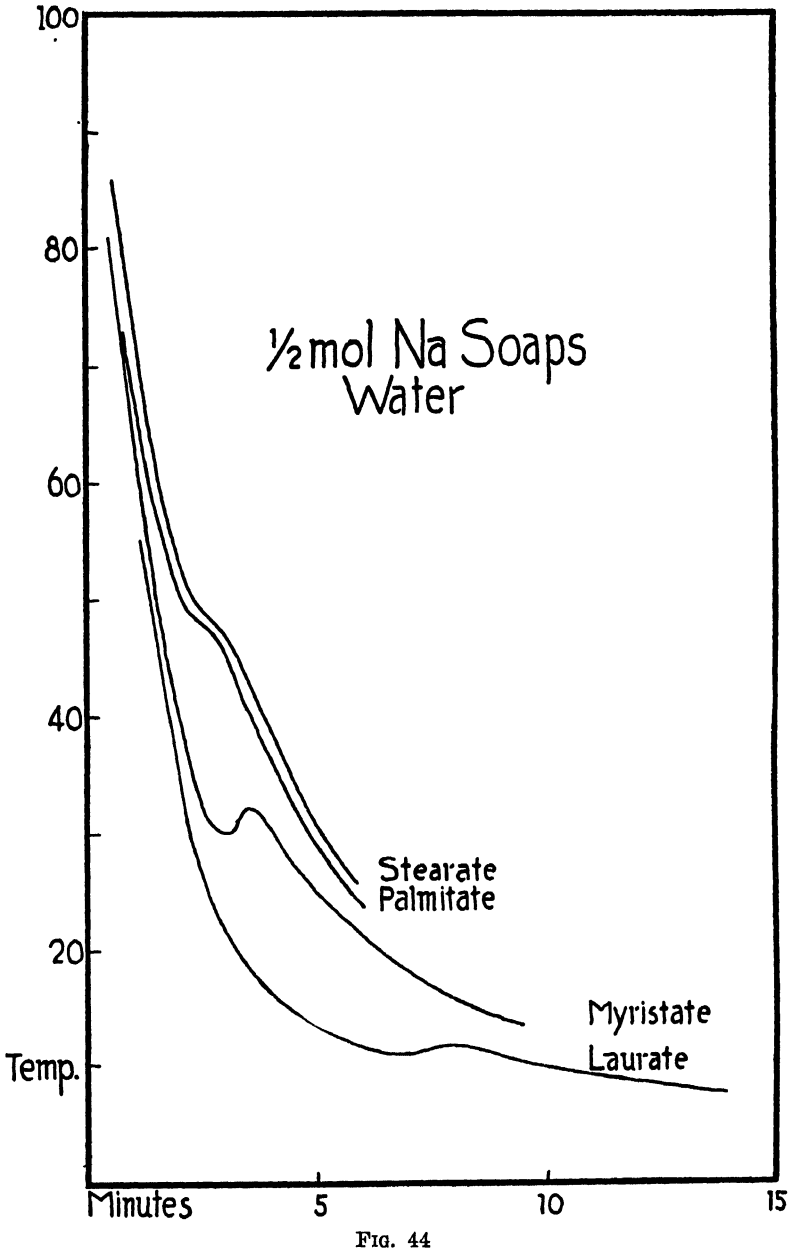

100
80
60
40
20
Temp.
½ mol Na Soaps
Water
Stearate
Palmitate
Myristate
Laurate
Minutes
5
10
15

FIG. 44

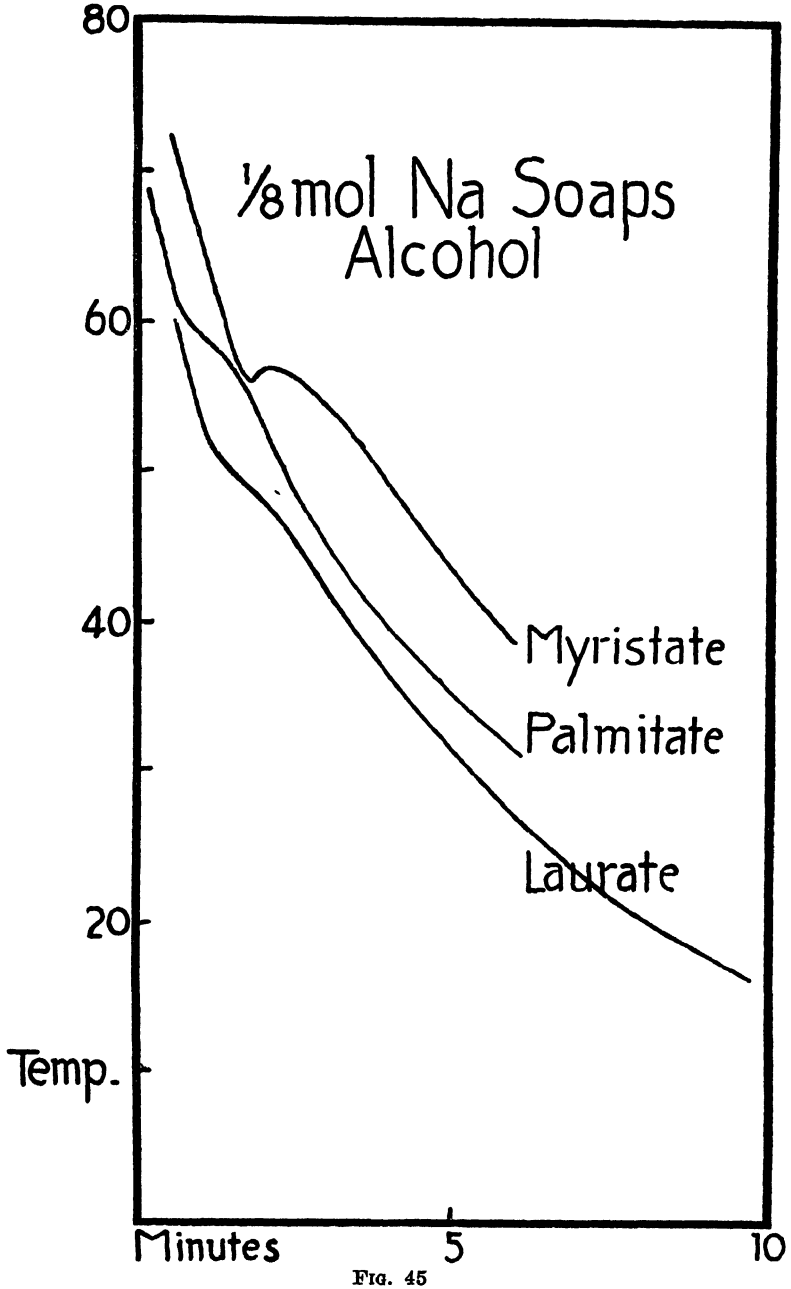

80
60
40
20
Temp.
⅛ mol Na Soaps
Alcohol
Myristate
Palmitate
Laurate
Minutes
5
10

FIG. 45

lated values are given under Δt in the various tables and Fig. 46 illustrates what such cooling curves look like.

The experiments described are readily reproducible and the curves obtained in duplicate runs are practically indentical.[46a] The breaks never fail to occur though their exact form, whether level in type or humped, is dependent upon the suddenness with which the gelatin occurs throughout the system. When this is great, the temperature actually rises for a time and a hump results, while when it is less abrupt, the curve of arrested fall in temperature takes its place.

Unless a lyophilic colloid passes rather rapidly from the one type of solution to the other, the liberation of heat occurs too gradually to make itself prominent in the course of a cooling curve. Slow setting colloids therefore show less irregularity in temperature drop than faster setting ones,[47] and those which are liquid/liquid mixtures at the final temperature show less change than those which are solid/liquid systems. Thus the curves for the potassium soaps show less irregularity than the corresponding ones for sodium soaps, and mixtures like caoutchouc/benzene exhibit relatively smooth curves which, however, lie higher than the cooling curves of their components. Mixtures of aluminium stearate with paraffin oils or various coal tar fractions (benzene, toluene, xylol, etc.)[48] show definite humps in the cooling curve but they are extended affairs owing to the slowness with which these materials dissolve *in* the metallic soap to yield "greases."[49]

[46a] We have repeated these experiments many times in the last several years registering the thermal changes electrically by use of a thermocouple and the recording device of Leeds and Northrup. The curves thus automatically registered are identical with those here described.

[47] J. FRANK, for example (Kolloidchem. Beih., *4*, 193 (1913)) could discover no measurable liberation of heat when gelatin gels; and H. FREUNDLICH (Kapillarchemie, 969, Leipzig, (1923)) holds that the temperature-time curve of every transition from sol to gel is perfectly smooth.

[48] See page 164.

[49] Since the first publication of our experimental findings that heat is set free in the process of gelation, it has been noted by A. LOTTERMOSER and W. MATTHAES (Kolloid-Zeitschr., *46*, 366 (1928)) in the instances of sodium palmitate and gelatin. Their experiments on gelatin (Zeitschr. f. physik. Chemie, *141*, 129 (1929)) take the place of the previously negative findings of FRANK.

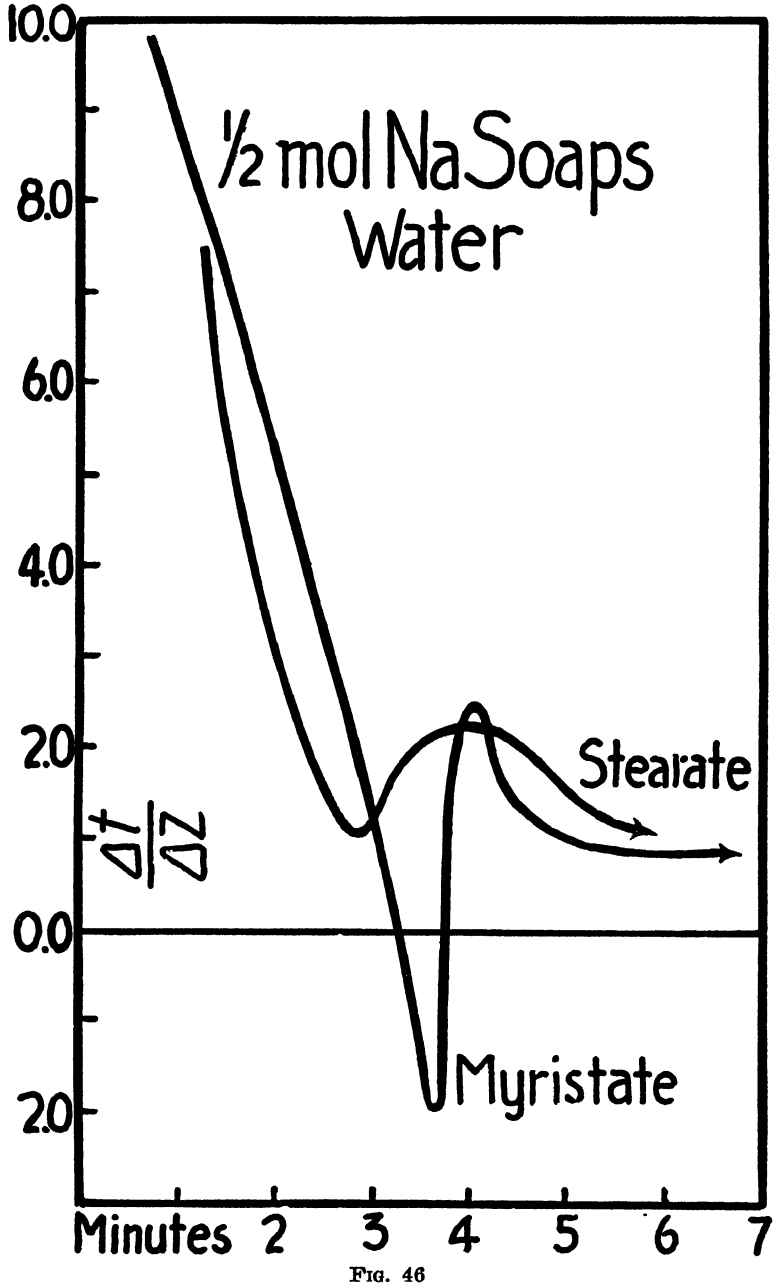

10.0
8.0
6.0
4.0
2.0
0.0
2.0
½ mol Na Soaps
Water
Stearate
Myristate
Δt/Δz
Minutes 2 3 4 5 6 7

FIG. 46

It is of interest to inquire into the nature of this exothermic activity. In connection with our general theory of the lyophilic colloid, it has been emphasized that, with lowering of temperature, the change from the original "true" solution of any material in a solvent is followed by supersaturation and so an agglomeration of the dissolved particles to colloid dimensions. If the solvent *cannot* dissolve in the colloid particles, a hydrophobic or lyophobic colloid results; but if it *can,* then a hydrophilic or lyophilic colloid is produced. To state the matter in different but synonymous terms, we may say that the colloid particle is not hydrated or solvated in the first instance, while in the second, it is. *Only when the colloid is hydrated or solvated is heat set free.*

In a first further analysis of such heat liberation, we may call to mind a fact of colloid chemistry. A colloid particle dissolving the solvent evidently increases in size, or "swells." Is such swelling the cause of the exothermic reaction when gelation occurs? This seems to be the case.

As long known from the classical observations of WIEDEMANN, LÜDEKING, HARDY, PAULI and others, the most varied types of hydrophilic colloids liberate heat when thrown into water to swell. We used this observation some years ago[50] to help explain the physiological fact that the temperatures of various gland secretions (rich in lyophilic colloids) frequently lie above those of the blood or the gland substance itself. It is partly responsible also for the increased temperatures registered in "injured" tissues or when these become "inflamed" (though the total calories yielded are too low to account for all such temperature rises).

To demonstrate the colloid chemical fact to our students, we have made use of the following experiments.

A small (50 cc.) oil extraction flask is fitted with a stopper carrying a good thermometer as illustrated in Fig. 47. The flask is filled two-thirds full of any hydrophilic colloid, and a graduate filled with water is set beside it. All the materials for an experiment are brought to the same temperature by being set together for a number of hours in a quiet spot in the laboratory.

[50] MARTIN H. FISCHER: Physiology of Alimentation, 182, New York, (1907).

When the experiment is to be made, an extra thermometer or two are used to verify the fact that colloid and water are of the same temperature. A proper amount of water (not more than can be quickly absorbed by the colloid) is now suddenly poured upon the hydrophilic colloid and, with the aid of the thermometer in the cork, the two are quickly stirred together. The cork is pushed into position, with the bulb of the thermometer buried in the cen-

TABLE LXXII.—*Maximal temperature increases registered when lyophilic colloids are permitted to swell*

Grams	Substance	Water in cc.	Temperature of all materials and apparatus when used	Maximum observed temperature after mixing	Temperature change
					° *C.*
10	finely powdered karaya gum	50	29.0	30.5	1.5
27.4	gum Arabic	25	32.5	36	3.5
33	Kahlbaum's soluble starch	25	27.5	33	5.5
29.5	cornstarch	25	31.5	35.5	4.0
32.6	tapioca	25	32.2	34	1.8
25	powdered blood fibrin	25	27.2	34.2	7.0
18.6	powdered egg white	20	32.0	34.6	2.6
14.3	aleuronat granules	35	31.5	34	3.5
30	dried milk powder	25	30.5	31.5	1.0
16	powdered gelatin	25	29.6	32.2	2.6
59.7	anhydrous lanolin	10	31.5	32.5	1.0
26	Portland cement	8	30.0	31.9	1.9
14	plaster of Paris	6	30.2	32.3	2.1

Dry soaps, interestingly enough, when first mixed with water or alcohol, show a *fall* in temperature (due to the solution of the soaps *in* the solvent ?), to be followed later by a rise above the original level.

ter of the swelling mass. The temperature rises immediately and is maintained many minutes (30 minutes to an hour) afterwards.

Table LXXII illustrates the temperature rises which may, in this fashion, be obtained. It serves to indicate also how common is the effect and how considerable the liberation of heat. A fact worth remembering in this connection is that swelling is *greater* at lower temperatures than at higher ones, that it is *increased*, in other words, if the mixture is made at lower temperatures. This

relation has been noted experimentally by J. W. McBain and C. S. Salmon[51] in the case of their "soap fibrils."

Having thus indicated the sameness between the heat of swelling of a lyophilic colloid and its heat of gelation, we wish to suggest that *these heats are identical with those observed whenever crystals solidify with water of crystallization.*

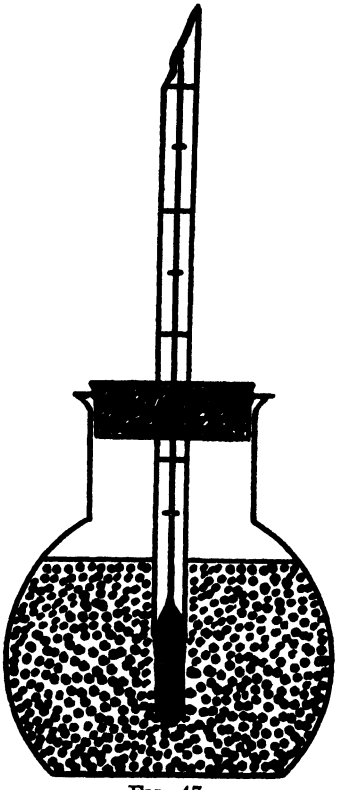


Fig. 47

The lyophilic colloids of the type here described appear in two of the rubrics of Wolfgang Ostwald's fundamental classification of the dispersed systems. They may be liquid/liquid mixtures (as when potassium oleate is mixed with water at ordinary temperatures) or they may be solid/liquid mixtures (as when sodium stearate is mixed with water). The two phases, water

[51] McBain and Salmon: Jour. Chem. Soc., *119*, 1374 (1921); see also the review of this field by A. Kuhn: Kolloid-Zeitschr., *35*, 275 (1924).

TABLE LXXIII.—*Cooling rate of four molten salts with water of crystallization*

Temperature of waterbath	13°		13°		12°		8°	
Minutes after immersion	$Al_2(NH_4)_2(SO_4)_4$ 24 H_2O		$AlK(SO_4)_2$ 12 H_2O		$MgSO_4$ 7 H_2O		$CaCl_2$ 6 H_2O	
	t	Δt	t	Δt	t	Δt	t	Δt
0	110		106		111		124	
15	95	15	86	20	90	21	99	25
30	77	18	74	12	74.5	15.5	84	15
45	74	3	65	9	95	−20.5	71	13
55	81	−7		−4		0.5		3.25
1	84	−3	73	−4	94	0.5	64.5	3.25
15	87.2	−3.2	79	−6	92	2	49	5.5
30	89	2	81.5	−2.5	87.5	4.5	43	6
45	90	1	83	−1.5	82.5	5	39	4
2	90	0	83.5	−0.5	79.5	3	35	4
15	89.8	0.2		0.5	76	3.5	32.5	2.5
30		0.35	82.5	0.5	74	2		3.16
45	89.1	0.35	81	1.5				3.17
3	88.5	0.6	78.5	2.5			23	3.17
15	87.5	1	76	2.5			23	0
30		1.5	72	4			25	−2
45	84.5	1.5	70	2			29	−4
4	80	4.5	66.5	3.5			30	−1
15	75	5		6.75			30	0
30	70	5	53	6.75			30	0
45	61.5	8.5					30	0
5	52.5	9					29.5	0.5
15		4.75						0
30	43	4.75						0
45								0
6							29.5	0
7							29.5	0
8							29	0.5
9							29	0
10							29	0
11							29	0
12							29	0
13							29	0
14							29	0
15							29	0
16							28.5	0.5
17							26.5	2
18							21	5.5

in soap and soap in water, are both liquid in the former instance (constitute mutually soluble *liquids*, in other words) but in the latter, one is solid (the solution of the water in sodium stearate

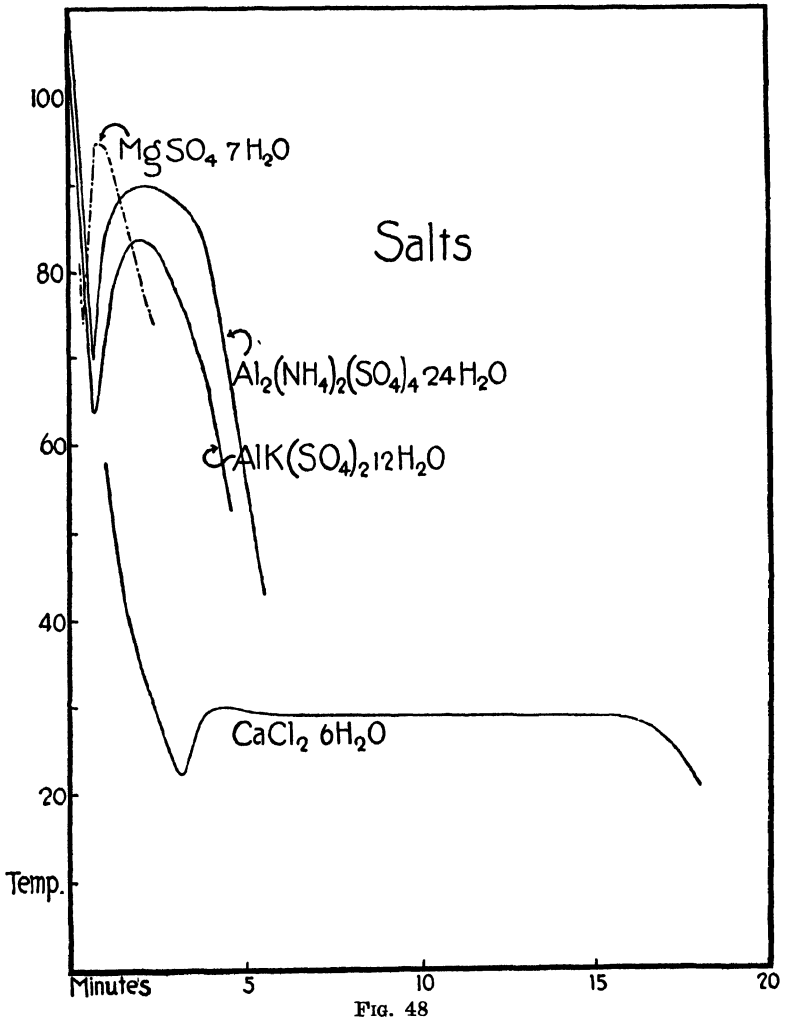


FIG. 48

being a crystal). In the production of such a solid phase out of the previously liquid one, two sources of heat must, in consequence, be considered—that incident to the change of a liquid to a solid, and that incident to the taking up of the "solvent" by

the solid. We look upon the water of crystallization which goes with a crystal of any kind as of the same type of "solid" solution of water *in* the crystal as is here discussed in conjunction with the general theory of the lyophilic colloid.

The crystals of salts like $CaCl_2 \cdot 6H_2O$, $MgSO_4 \cdot 7H_2O$, $AlK(SO_4)_2$ $12H_2O$, and $Al_2(NH_4)_2(SO_4)_4$ $24H_2O$ hold large fractions of their "solvent" in "solid" solution within themselves and in this form correspond to the solidified hydrophilic colloids which interest us. But these salts are also so readily soluble in water that, when heated, they dissolve in their own waters of crystallization (corresponding in this form to our lyophilic colloids in a "dissolved" state). That the salts are practically molecularly dissolved in their waters of crystallization is proved by the fact that the molten crystals boil at but a few degrees above the boiling point of water. We append Fig. 48 (drawn from the data contained in Table LXXIII) to illustrate how these crystal melts fall in temperature when plunged into a cold water bath. When such hot solutions, treated as the lyophilic colloid systems above described, are chilled, their temperature drops rapidly to a low point when, in spite of continuous immersion—it is of interest colloid-chemically that in this zone the mixtures become syrupy and slightly opalescent—their temperature suddenly rises again as crystallization sets in, to fall a second time as this "heat of crystallization" is lost to the water bath. The curves of Fig. 48 illustrate this physico-chemical fact better than many words.

IX. Application of the Theory of the Lyophilic Colloid to Some Specific Instances

We shall now try to illustrate how the theory of the lyophilic colloid as developed in the preceding pages helps us towards a simpler understanding of the "behavior" of such systems. Three colloid systems, namely, casein/water, silicic acid/water and metallic soap/hydrocarbons, receive detailed discussion though what is said for them may be applied by the reader to any other lyophilic colloid system with which he may be more familiar.

The first of these examples is chosen because it has to do with an "electrolyte" and water. Such systems are today the sheet

anchors of those hypotheses of colloid behavior which utilize electrical notions to explain such behavior; and since we hold that these have little or nothing to do with the case, they are used as a first material in illustration of the better applicability of the mutual solution concept. The third example is chosen because, while it still concerns various electrolytes, they are weak illustrations of this class and they are mixed with liquids generally looked upon as possessing little or no powers of electrolytic dissociation, namely, different paraffin oil fractions or other "organic solvents" which in the older days of physical chemistry, considered from any "electrical" point of view, were the deadest on the chemist's shelves. And yet, as we shall see, they yield the most typical of lyophilic colloid systems.

If the theory of the lyophilic colloid proposed in these pages is correct, *it should be possible to discover and produce at will in any lyophilic colloid/solvent mixture any of the four systems illustrated in the two diagrams of Fig. 2 and described on page* 4 (a solution of x in a solvent, followed by a colloid dispersion of solvated particles in the true solution, followed by a dispersion of the true solution within the solvated material as an external phase and ending in a true solution of the solvent in x). *It should also prove possible to change from the one to the other through simple variation* (*a*) *in the concentration of the constituents or* (*b*) *the temperature* (provided that the mutual solubilities are sufficiently affected by such temperature change, or, to use WOLFGANG OSTWALD'S term, provided that the materials constituting the lyophilic colloid system are sufficiently thermovariable). The succeeding pages illustrate these general truths.

A. The System Casein/Water[52]

1. *The water absorbing capacity of casein and some caseinates*

We used for our experiments the practically ash free (0.59 percent) Harris casein. This material, when air dry, carries about 10 percent water and combines readily with acids or alkalies to yield beautiful clear gels.

1. The stock material when thrown into water absorbs some 250 percent of its own weight of water. When *less* than this

[52] MARTIN H. FISCHER and MARIAN O. HOOKER: Kolloid-Zeitschr., *47*, 193 (1929).

amount of water is added to a given weight of the dry material, the whole becomes a glutinous mass constituting, in this state, to use our terminology, a solution of the water in the "neutral" casein. The "molecular" solubility of the water in the casein is therefore low.

The similar solubility of the casein in water is also low—the clear filtrate from a casein/water mixture gave no qualitative tests for protein. This is, to use again our terminology, the measure of the solubility of the neutral casein *in* water. The two solutions constitute, respectively, the zones Z and A of Fig. 2 (diagram B). What they look like in nature is apparent in any of the bottles marked H_2O in Fig. 49.

What does consideration of such a "neutral" casein/water mixture teach us that may be of significance for the general theory of the lyophilic colloids? *Whenever two materials show such a low degree of mutual solubility, they show also little tendency to yield those two mixed middle systems (sols and gels) which are the ones which give the lyophilic colloids their outstanding characteristics.* We shall see immediately that when the degree of such mutual solubility is heightened, as by the conversion of the neutral casein into a basic or acid deriative, the tendency to form gels or sols is also increased. And yet to obtain lyophilic colloid systems this may not be increased indefinitely. When the mutual solubility is *too great,* the middle systems again tend to disappear (as when alcohol is mixed with water) the result being that lyophilic colloids are again not obtainable (but only two "true" solutions which in common parlance are "readily miscible in all proportions").

2. The water absorbing capacity as well as the solubility of the casein *in* water is enormously heightened through addition of an acid or an alkali. This well-known fact is illustrated in Fig. 49 which shows the effect of adding a series of equinormal equivalents of different acids to a unit weight (12.5 grams) of casein in the presence of a constant volume of water (100 cc.).

All the mixtures were treated in identical fashion. After being set to soak in an ice-box for twenty-four hours, the mixtures were heated with careful stirring for one hour in a boiling water bath, and were then returned to the ice-box. The photographs

were made in each instance twenty-four hours after such treatment and at the temperature of the ice-box (6°).

The control bottles marked H_2O illustrate the amount of water absorbed by the pure casein. The addition of acid obviously leads to increased water absorption, but this effect varies with (a) the concentration and (b) the kind of acid used.

A first tendency to form a gel is apparent with hydrochloric acid (3/100 n). The bottle contents (second bottle in the second row from the top of Fig. 49) have gelled, but the gel is still opaque. A transparent gel is obtained when the concentration of the hydrochloric acid is raised to 4/100 n (second bottle of the third row). But at this concentration hydrobromic and nitric acids prove equally effective (third and fourth bottles of the third row). Lactic, formic and phosphoric acids also yield gels though not yet of a transparent type. When still higher concentrations of the acid are employed (6/100 n) the originally effective acids continue effective, formic and phosphoric yield clear gels, and malonic, tartaric and mendelic acids now also yield gels though opaque in type (fourth row).

Fig. 49 shows how, with still greater increase in concentration of the added acids, this tendency to yield gels moves increasingly toward the right; oxalic acid moves into the number yielding transparent gels at the 8/100 n level (fifth row) while at the 20/100 n concentration of the acid, (second row from the bottom) even citric acid becomes effective. *It should be noted that nowhere in the series does sulphuric acid become effective in yielding a gel;* even in the concentration 50/100 n the casein has swollen little more than in water, though at this concentration even acetic acid yields a clear gel (bottom row of Fig. 49).

The experiments illustrated in Fig. 49 show that a definite weight of practically anhydrous, non-swelling, neutral casein may, through the addition of a requisite amount of certain acids be converted into a water-absorbing material which, with the quantities of water here offered, sets to a clear gel. *Contrary to the generally accepted notion that the acid "influences" the protein and so causes it to swell or gelatinize, we would say that the effective acids combine with the neutral casein to yield casein chlorid, bromid, etc., and that the new compounds thus formed*

have a greater solubility for water than the original neutral casein.[53]

We have known since those first observations of S. BUGARSZKY and L. LIEBERMANN[54] and from their many successors that the proteins in the presence of various acids combine with these to yield salt-like derivatives. These salt-like derivatives differ, obviously, as to the acid radical which is carried into them through the added acid. As these differ *the protein salts have each for themselves a specific solubility in water and a specific solubility for water.*

Obviously, *the concentration of hydrogen ions*—a factor which is still being carried into the discussion of the effects of acids upon colloid behavior—*is not the effective agent;* for while a strong acid like hydrochloric or hydrobromic is found most effective in the production of a gel, the same hydrogen-ion concentration or a very much higher one derived from the use of sulphuric acid nowhere yields a gel. On the other hand, such obviously "weak" acids as lactic, formic, tartaric, mandelic and even acetic are so effective that at certain concentrations they do not fall much behind the gel producing "strong" acids.

3. Fig. 50 illustrates the effects of adding different gram equivalents of different alkalies to a given weight (12.5 g.) of neutral casein, again in the presence of a constant volume (100 cc.) of water. The experimental procedure was as in the case of the acids. The control bottles containing casein and water only are marked H_2O. With 4/100 n alkali (the top row of bottles) practically transparent gels are obtained with ammonium, potassium, sodium and lithium hydroxids. Calcium and barium hydroxids also yield gels at this concentration but these are whiter and less firm. It should be noted that at this concentration all the experimental mixtures still show a white (unneutralized?) sediment of casein.

In the next higher concentration (6/100 n) this white sediment disappears and all the bottles are filled with a transparent gel with the exception of the barium bottle which continues white (second row). Still higher concentrations (8/100 and 10/100 n) of

[53] See MARTIN H. FISCHER: Soaps and Proteins, 205, New York (1921).

[54] S. BUGARSZKY and L. LIEBERMANN: Pflüger's Arch. *72*, 51 (1898).

alkali do not change the total picture (the third and last rows of bottles in Fig. 50).

In interpretation of what has been described, we must again emphasize that *the alkalies have not merely "influenced" the neutral casein to increased swelling but have combined with this to form ammonium, potassium, sodium, etc., caseinates, each of which compounds has a greater solvent power for water (a greater hydration capacity) than the "neutral" casein.*

This set of experiments must also make it obvious that *the observed change in colloid behavior* (be it called an increased water absorption by the casein or an increased tendency to form a gel, or an increase in the tendency of the casein to peptize, or what not) *is in no fundamental fashion a function of the concentration of the hydroxyl ions.* Ammonium hydroxid is seen to be as effective as potassium or sodium hydroxids and both of these are more effective than the equally strong calcium or barium hydroxid. It seems to us, therefore, that it is more correct to say that these hydroxids have combined with the casein to form basic caseinate compounds (analogous to the basic fatty acids compounds which we call soaps) and that, depending upon the nature of the base which has been introduced into the casein, a series of derivatives has been obtained each again possessed of its specific solvent power for water (and its specific solubility in water).

4. When the gels are compared which result when a given weight of casein is combined with a given amount of alkali or the chemical equivalent of acid, it is found that the base-casein compound is more fluid than the corresponding acid-casein compound. In the terminology which we are using we may explain this difference by saying (a) that the hydrated base-casein compounds are more liquid at ordinary temperatures than are the equally concentrated acid-casein compounds (tend, in other words, to yield liquid/liquid systems as illustrated in A of Fig. 2 instead of the solid/liquid systems shown in B) and (b) that the basic compounds are not only more soluble in water but have a lesser capacity for dissolving water, (for combining with water to form a hydrate) than the comparable acid compounds.

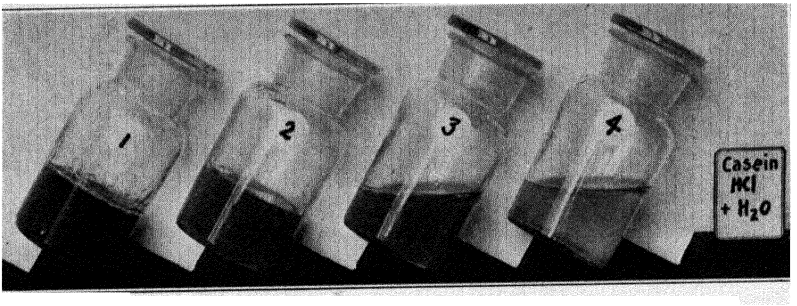

1
2
3
4
Casein
HCl
+ H2O

FIG. 51

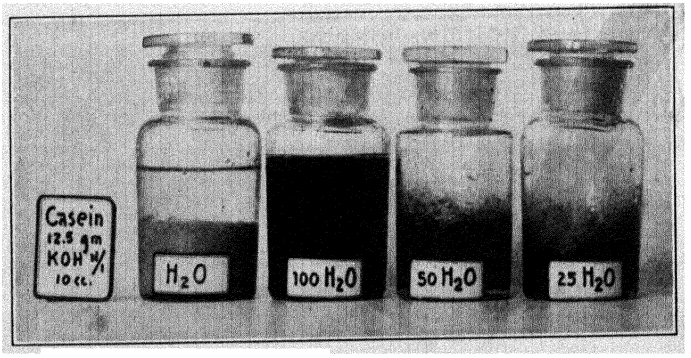

Casein
12.5 gm
KOH 1/1
10 cc.
H2O
100 H2O
50 H2O
25 H2O

FIG. 52

A measure of the factor (b) is given in Figs. 51 and 52. Fig. 51 shows, in the bottle labelled 1, the solid, gelatinous character at 5° of the system produced by treating 12.5 grams of casein with 100 cc. 1/10 n HCl. When this gel is diluted with 25 percent, 50 percent and 75 percent water, as shown in bottles 2, 3, 4, the mixture is first thickly viscid, then viscid, and finally as mobile as milk.

In Fig. 52 the bottle marked 100 H_2O represents the syrup-like gel which results when 12.5 grams casein are treated with 100 cc. 1/10 n KOH. If the water in this mixture is *reduced* by half (the bottle marked 50 H_2O) a stiff gel is formed; and if reduced by 75 percent (the bottle marked 25 H_2O) a shellac-like solid is obtained.

These two sets of experiments indicate, therefore, that, *depending upon the concentration of water in the total system, everything may be obtained from the extreme, on the one hand, of what approximates a true solution of the caseinate in the water through a sol and a gel to what, at the other extreme, is apparently a dry "solution" of the water in the caseinate.* With fixed concentration of the water in the system a similar run from solution of the caseinate in the water to one of the water in the caseinate is accomplished through mere temperature change. As evidenced in the preparation of any of the caseinates here described there may be produced at the temperature of a boiling water bath a caseinate/water system which is as clear as water and non-viscid and which with falling temperature becomes opalescent, increasingly viscid and finally sets into a solid gel.

2. *The effects of salts and non-electrolytes upon some caseinates*

Having shown in this fashion where any alkali caseinate/water system or any acid caseinate/water system finds its place in the general diagrams of Fig. 2, we wish next to describe the effects of adding various electrolytes to such systems. Such additions affect the viscosity of these systems, their optical properties, their gelation and their precipitation. The explanation of such salt action is usually electrical in type. Since we hold that such electrical action—like the action of ions—has little or nothing to do with the case, for in properly chosen examples of lyophilic colloids the non-electrolytes prove as effective or more

effective than the electrolytes, we venture to repeat here the notions originally advanced to explain the stabilization of hydrophilic colloids through increased hydration and their precipitation through dehydration as developed for various soaps and proteins.[55]

We will begin with a description of the effects of various electrolytes upon the "behavior" of an acid-casein (casein hydrochlorid) and three base-caseins (ammonium, potassium and sodium caseinates).

The effect of adding KCl to a sol of casein chlorid is shown in Fig. 53 and Table LXXIV. The stock casein chlorid/water system was prepared in the usual manner by adding 100 cc. 1/10 n HCl to 12.5 grams of casein. The originally liquid casein chlorid/water system shown in tube 1 becomes increasingly viscid, with increasing concentration of the added salt, until it sets into a gel in tubes 4 and 5; separation into "clot" and "serum" is apparent in tube 6, and becomes complete in tube 7 to the end of the series.

Fig. 54 shows that the same is true when chemical equivalents of NaCl take the place of KCl. It needs merely to be noted that the sequence of changes is shifted slightly to the left, beginning separation into clot and serum being apparent in tube 5.

When now K_2SO_4 takes the place of KCl in the same casein chlorid/water mixture, the described effects are all re-enacted, but the effect of the sulphate (in terms of *normality*) is roughly ten times or (in terms of *molar* concentration) twenty times as great. The molar concentration of the salt in the tubes of Fig. 55 and in Table LXXV is one twentieth that in the corresponding tubes of Figs. 53 and 54. Nevertheless, gelation is apparent in tubes 8 and 9, and separation is complete in tubes 10 and 11.

Fig. 56 and Table LXXVI show the effect of adding trisodium citrate to casein chlorid. We deal, in this series, with the disturbing effects of the addition of a distinctly alkaline salt to an acid caseinate. There is still discoverable, however, the same sequence of increase in viscosity to gelation followed by separation of a clot with the production of "serum" as in the already described experiments. Comparison of the tubes containing any given concentration of sulphate with that of a citrate is difficult

[55] MARTIN H. FISCHER: Soaps and Proteins, 205, New York (1921).

TABLE LXXIV.—*Casein chlorid + potassium chlorid*

	Mixture	Remarks
(1)	10 cc. casein chlorid + 5.0 cc. H_2O (control)	liquid
(2)	10 " " " + 0.5 cc. 1/1 m KCl + 4.5 cc. H_2O	liquid
(3)	10 " " " + 1.0 " " " " + 4.0 " "	liquid but less transparent
(4)	10 " " " + 1.5 " " " " + 3.5 " " ..	soft gel
(5)	10 " " " + 2.0 " " " " + 3.0 " " ..	" "
(6)	10 " " " + 2.5 " " " " + 2.5 " " .	syneresis with separation of a caesin clot
(7)	10 " " " + 3.0 " " " " + 2.0 " "	separation of casein clot complete
(8)	10 " " " + 3.5 " " " " + 1.5 " "	" " "
(9)	10 " " " + 4.0 " " " " + 1.0 " " .	" " "
(10)	10 " " " + 4.5 " " " " + 0.5 " " .	" " "
(11)	10 " " " + 5.0 " " " "	" " "

TABLE LXXV.—*Casein chlorid + potassium sulphate*

	Mixture	Remarks
(1)	10 cc. casein chlorid + 5.0 cc. H_2O (control) .	liquid
(2)	10 " " " + 0.5 cc. 1/20 m K_2SO_4 + 4.5 cc. H_2O	liquid
(3)	10 " " " + 1.0 " " " " + 4.0 " "	"
(4)	10 " " " + 1.5 " " " " + 3.5 " " ..	"
(5)	10 " " " + 2.0 " " " " + 3.0 " " .	"
(6)	10 " " " + 2.5 " " " " + 2.5 " " ..	" but less transparent and more viscid
(7)	10 " " " + 3.0 " " " " + 2.0 " " .	soft gel
(8)	10 " " " + 3.5 " " " " + 1.5 " " .	solid gel
(9)	10 " " " + 4.0 " " " " + 1.0 " " .	" "
(10)	10 " " " + 4.5 " " " " + 0.5 " " ..	separation of curd
(11)	10 " " " + 5.0 " " " "	" " "

TABLE LXXVI.—*Casein chlorid + trisodium citrate*

Mixture	Remarks
(1) 10 cc casein chlorid + 5.0 cc H_2O (control)	liquid
(2) 10 " " " + 0.1 " 1/6 m trisodium citrate + 4.9 cc H_2O	"
(3) 10 " " " + 0.3 " " " " " + 4.7 " "	"
(4) 10 " " " + 0.4 " " " " " + 4.6 " "	" but more viscid
(5) 10 " " " + 0.5 " " " " " + 4.5 " "	soft gel
(6) 10 " " " + 0.6 " " " " " + 4.4 " "	gel with slight syneresis
(7) 10 " " " + 0.7 " " " " " + 4.3 " "	beginning separation
(8) 10 " " " + 1.0 " " " " " + 4.0 " "	separation complete
(9) 10 " " " + 2.0 " " " " " + 3.0 " "	" "
(10) 10 " " " + 3.0 " " " " " + 2.0 " "	" "
(11) 10 " " " + 4.0 " " " " " + 1.0 " "	" "
(12) 10 " " " + 5.0 " " " " "	" "

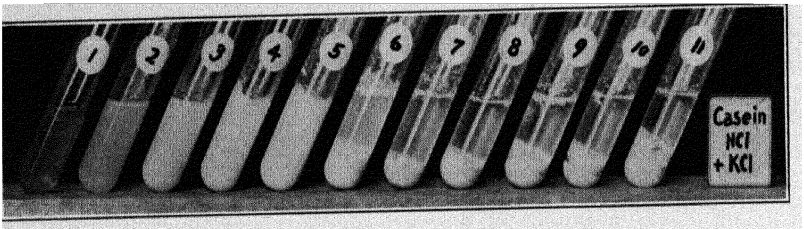


FIG. 53

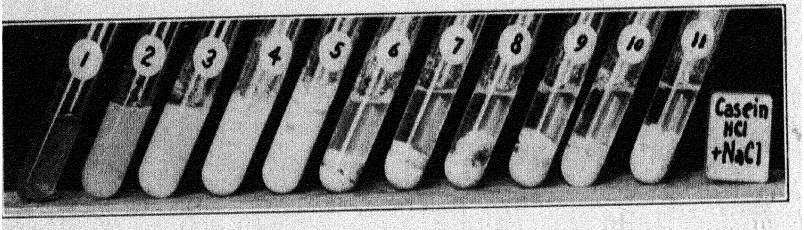


FIG. 54

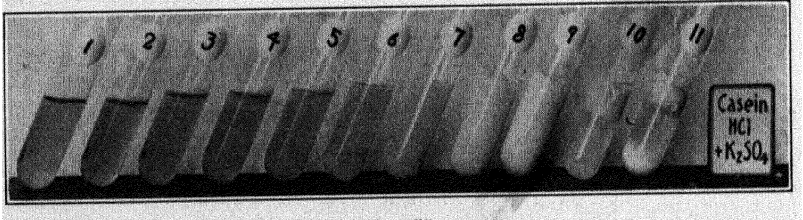


FIG. 55

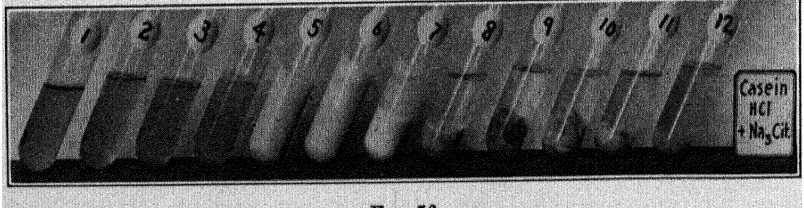


FIG. 56

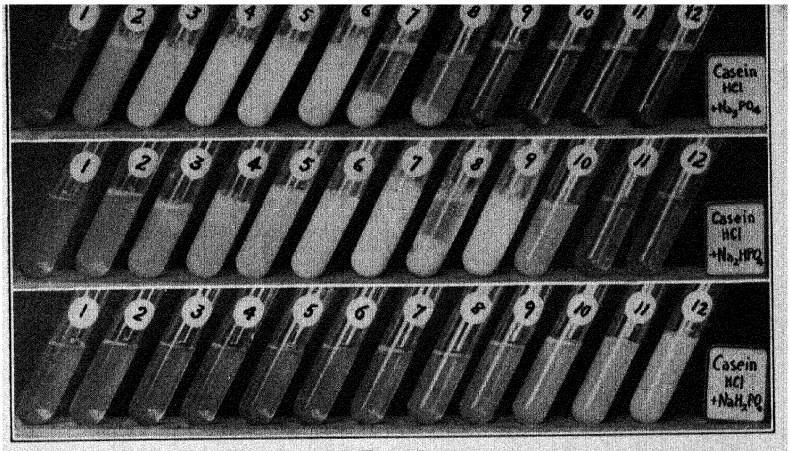


FIG. 57

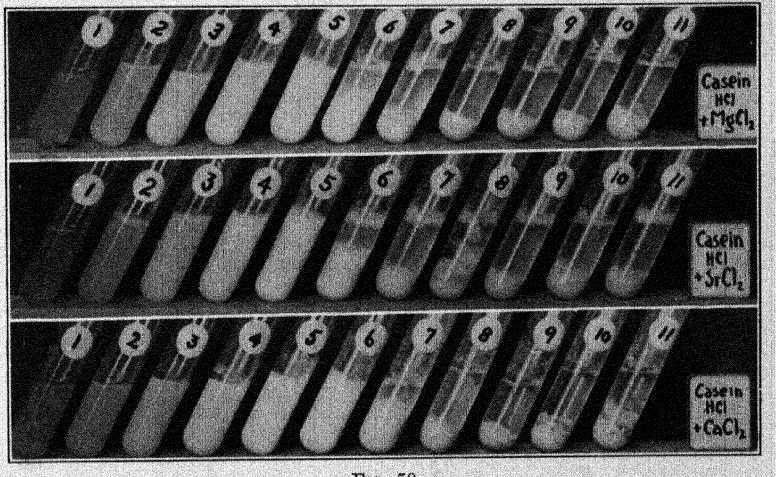


FIG. 58

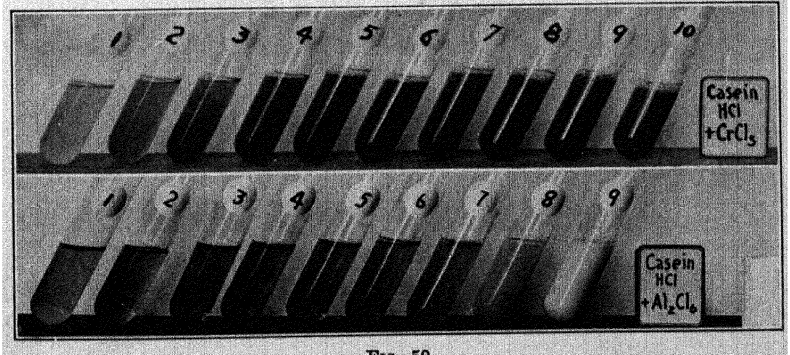


FIG. 59

because of the alkaline nature of the trisodium citrate, but if we make allowance for this (see the next paragraph on phosphates) this group of experiments with chlorids, citrates and sulphates suffices to show that in the production of the described effects, the acid radicals contained in the salts follow this order when that least effective is named first. A look at Fig. 49 shows that this is the inverse of the order in which the pure acids hydrate "neutral" casein.

The effects of the same molar concentration of the three different sodium phosphates upon casein chlorid are shown in Fig. 57 and Table LXXVII. The alkaline trisodium phosphate series is shown in the top row, so that the tubes 2, 3, 4, 7, 10, 11 and 12 may be compared with the similarly concentrated tubes 5, 6, 7, 8, 10, 11, 12, of the citrate series (Fig. 56 and Table LXXVI). While both these trivalent salts produce the same primary set of viscosity, gelation and separation changes and at about the same concentration, the phosphate series shows a stronger tendency to put the casein "back into solution" in the end tubes. We emphasize the fact because the *acid* radicals of the salts here again follow the order of the pure acids (see Fig. 49) in this regard. When disodium phosphate replaces the trisodium salt, the sequence of changes is the same but moves toward the right, and with the monobasic salt this shift becomes so great that only soft gelation is discovered in the series of concentrations here employed.

In Fig. 58 and Table LXXVIII are shown the effects of adding molar equivalents of the chlorids of magnesium, strontium and calcium to casein chlorid. The quantitative effects and the sequence of changes produced by the three different salts are the same. These effects are identical with those produced by NaCl (see Fig. 54) of twice the molar concentration.

In Fig. 59 are shown the effects of chromium chlorid and aluminium chlorid upon casein chlorid. In both sets there is apparent a gradual increase in viscosity until a soft gel is formed in the last tube of each series, in which the final concentration of the salt, after mixing with the casein, is 1/18 m. This concentration is comparable to that of the sodium chlorid in the tube marked 5 of Fig. 54.

TABLE LXXVII.—*Casein chlorid + sodium phosphate*

Mixture	Na_3PO_4	Na_2HPO_4	NaH_2PO_4
(1) 10 cc casein chlorid + 5.0 cc H_2O (control)	liquid	liquid	liquid
(2) 10 " " " + 0.5 " 1/6 m phosphate + 4.5 cc H_2O	viscid		
(3) 10 " " " + 0.6 " " " " + 4.4 " "	soft gel		
(4) 10 " " " + 0.7 " " " " + 4.3 " "	separation		
(5) 10 " " " + 0.8 " " " " + 4.2 " "	separation increases	increasing viscosity	
(6) 10 " " " + 0.9 " " " " + 4.1 " "	"	soft gel	
(7) 10 " " " + 1.0 " " " " + 4.0 " "	separation complete	" "	
(8) 10 " " " + 1.5 " " " " + 3.5 " "	re-solution begins	separation	
(9) 10 " " " + 2.0 " " " " + 3.0 " "	re-solution complete	beginning re-solution	
(10) 10 " " " + 3.0 " " " " + 2.0 " "	"	complete re-solution	
(11) 10 " " " + 4.0 " " " " + 1.0 " "	"	" "	gradually increasing viscosity with loss of transparency
(12) 10 " " " + 5.0 " " " " " "	"	" "	soft gel
(13) 10 " " " + 1.0 " 1/1 m phosphate + 4.0 " "			beginning separation
(14) 10 " " " + 2.0 " " " " + 3.0 " "			complete separation
(15) 10 " " " + 3.0 " " " " + 2.0 " "			

Taken together, these experiments show that the effects in increasing viscosity to the point of gelation with subsequent salting out of casein chloride for a series of monovalent, divalent and trivalent chlorids stand in the relation 1 : 1/2 : 1/3 when the bases are compared, or as 1 : 1 : 1 when the chlorid concentrations are compared. This is the relation between precipitating effect and electric charge of the ions which various authors since the

TABLE LXXVIII.—*Casein chlorid + magnesium, or strontium, or calcium chlorid*

	Mixture			Remarks
(1)	10 cc casein chlorid	+ 5.0 cc H_2O (control)	.....	liquid
(2)	10 " " "	+ 0.5 " 1/5 m salt sol.	+ 4.5 cc H_2O	more viscid
(3)	10 " " "	+ 1.0 " " " " "	+ 4.0 " "	" "
(4)	10 " " "	+ 1.5 " " " " "	+ 3.5 " "	soft gel
(5)	10 " " "	+ 2.0 " " " " "	+ 3.0 " "	" "
(6)	10 " " "	+ 2.5 " " " " "	+ 2.5 " "	separation
(7)	10 " " "	+ 3.0 " " " " "	+ 2.0 " "	begins further
(8)	10 " " "	+ 3.5 " " " " "	+ 1.5 " "	separation separation
(9)	10 " " "	+ 4.0 " " " " "	+ 1.0 " "	complete "
(10)	10 " " "	+ 4.5 " " " " "	+ 0.5 " "	"
(11)	10 " " "	+ 5.0 "		"

days of W. B. HARDY have used as proof that the colloid precipitation was electrical in nature, and yet, as will be shown immediately, the explanation is simpler.

2. We pass now to the effects of various salts upon the *alkali* caseinates. It will be seen that in this instance also those salts which do not react chemically with the alkali caseinate increase its viscosity to a maximum (make it gel if not too much water is present in the system) and then salt it out as a clot. When the salt *can* react with the alkali caseinate, the fundamental picture

remains the same, only the properties of the initial system are simultaneously affected—an alkali caseinate of initially *higher* hydration capacity and solubility in water being produced, for example, if a neutral potassium salt is added to a calcium caseinate, and one of *lower* hydration capacity and lower solubility in water if a neutral calcium salt is added to a potassium caseinate.

The upper row of Fig. 60 shows that a sodium caseinate/water system (12.5 grams casein + 100 cc. 1/10 n NaOH) prepared in

TABLE LXXIX.—*Sodium caseinate + sodium or potassium chlorid*

	Mixture	NaCl	KCl
(1)	10 cc Na caseinate (control)	liquid	liquid
(2)	10 " " " + 0.004 mol. salt .	increasing viscosity	increasing viscosity
(3)	10 " " " + 0.008 " "	gel	"
(4)	10 " " " + 0.012 " "	"	"
(5)	10 " " " + 0.016 " "	"	"
(6)	10 " " " + 0.020 " "	"	"
(7)	10 " " " + 0.024 " "	"	soft gel
(8)	10 " " " + 0.028 " "	"	" "
(9)	10 " " " + 0.032 " "	"	" "
(10)	10 " " " + 0.036 " "	"	" "
(11)	10 " " " + 0.050 " "	"	beginning separation
(12)	10 " " " + 0.066 " "	syneresis	salted out
(13)	10 " " " + 0.088 " "	salted out	" "
(14)	10 " " " + 0.100 " "	" "	" "

the standard fashion and itself liquid, becomes increasingly viscid, upon the addition of a dry salt like NaCl,[56] until a gel is formed. Upon further addition of NaCl, separation into a "clot" and "serum" takes place.

The lower row of Fig. 60 shows that similar effects are produced by molecularly equivalent concentrations of KCl, though the points at which the described succession of changes occurs are slightly shifted to the right. This effect is explained through the formation of some potassium caseinate by double decomposition,

[56] The dry salt is used because the addition of water, through use of a salt solution, so dilutes the total system that the hydration capacity of the alkali caseinate is exceeded and so the formation of a gel made impossible.

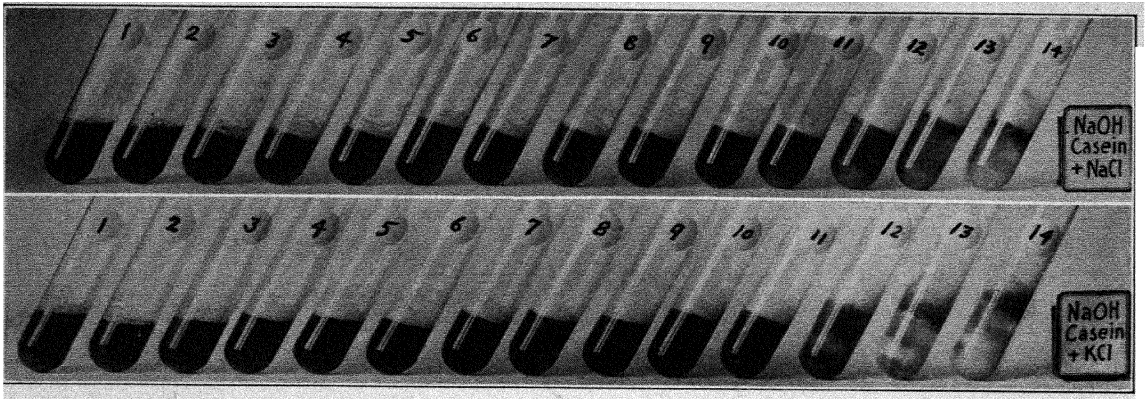

1 2 3 4 5 6 7 8 9 10 11 12 13 14
NaOH
Casein
+NaCl
1 2 3 4 5 6 7 8 9 10 11 12 13 14
NaOH
Casein
+KCl

FIG. 60

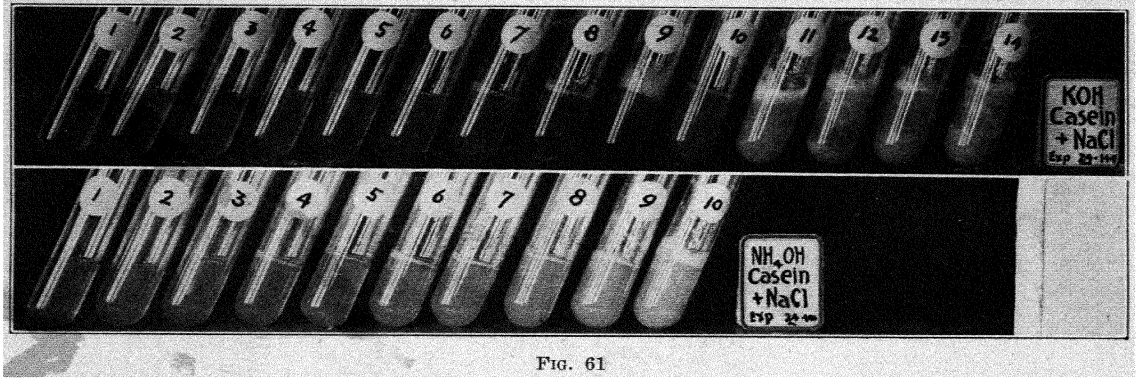

1 2 3 4 5 6 7 8 9 10 11 12 13 14
KOH
Casein
+NaCl
1 2 3 4 5 6 7 8 9 10
NH4OH
Casein
+NaCl

FIG. 61

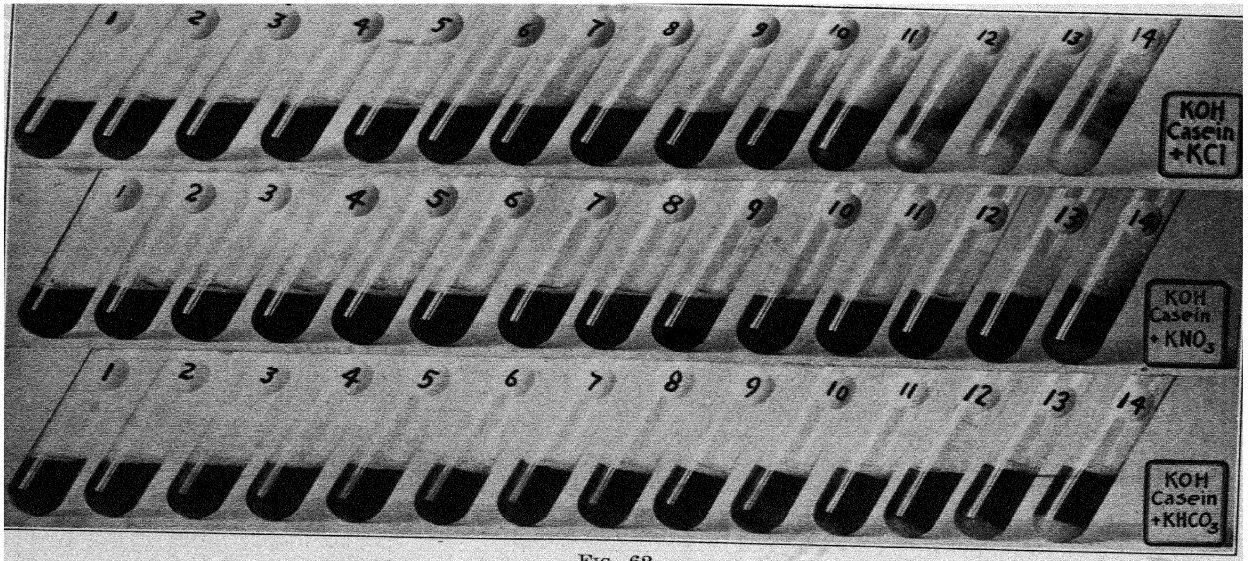

1 2 3 4 5 6 7 8 9 10 11 12 13 14
KOH Casein +KCl
1 2 3 4 5 6 7 8 9 10 11 12 13 14
KOH Casein + KNO_3
1 2 3 4 5 6 7 8 9 10 11 12 13 14
KOH Casein + $KHCO_3$

FIG. 62

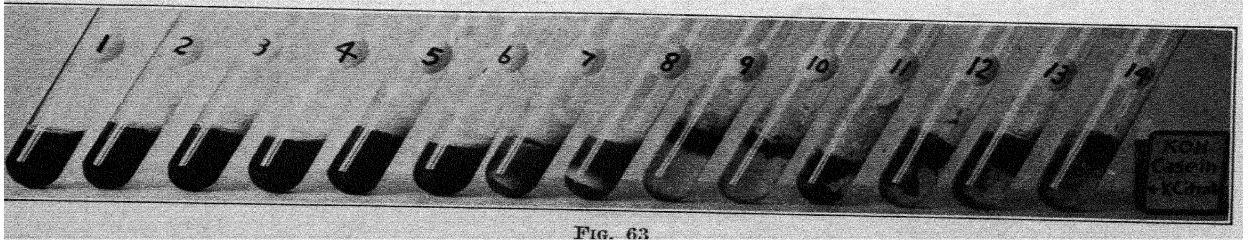

1 2 3 4 5 6 7 8 9 10 11 12 13 14
KOH Casein +KCl

FIG. 63

a view supported by the findings in the upper row of Fig. 61 in which potassium caseinate had sodium chlorid added to it. It will be noted that while concentrations, temperature, etc., were identical, gelation was not apparent until tube 5 was reached, while it occurred in tube 3 in the upper row of Fig. 60 in which sodium caseinate had NaCl added to it. Ammonium caseinate in its behavior stands closer to potassium caseinate than to sodium caseinate, as apparent from the lower row of tubes in Fig. 61. The numerical details covering Figs. 60 and 61 are found respectively in Table LXXIX and LXXX.

TABLE LXXX.—*Potassium or ammonium caseinate + sodium chlorid*

	Mixture	Potassium Caseinate	Ammonium Caseinate
(1)	10 cc. caseinate (control) ..	liquid	liquid
(2)	10 " " + 0.004 mol. NaCl	increasing viscosity	increasing viscosity
(3)	10 " " + 0.008 " "	" "	" "
(4)	10 " " + 0.012 " "	" "	" "
(5)	10 " " + 0.016 " "	solid clear gel	solid clear gel
(6)	10 " " + 0.020 " "	" " "	" " "
(7)	10 " " + 0.024 " "	" " "	" " "
(8)	10 " " + 0.028 " "	" " "	" " "
(9)	10 " " + 0.032 " "	" " "	" " "
(10)	10 " " + 0.036 " "	" " "	" " "
(11)	10 " " + 0.050 " "	beginning separation	
(12)	10 " " + 0.066 " "	increasing separation	
(13)	10 " " + 0.088 " "	" "	
(14)	10 " " + 0.100 " "	" "	

Fig. 62 shows in the successive rows the effects, respectively, of potassium chlorid, nitrate and bicarbonate upon a standard potassium caseinate/water system (12.5 grams casein + 100 cc. 1/10 n KOH). The numerical details are given in Table LXXXI. Fig. 63 shows the effects of potassium citrate. The molar concentrations of this salt were lowered so that tube 5 in the series corresponds with tube 2 of Fig. 62, and tube 9 with tube 3. Table LXXXII gives the details.

These experiments suffice to show that, at the same molar concentration, different acid radicals bring about the succession

TABLE LXXXI.—*Potassium caseinate + different potassium salts*

Mixture	KCl	KNO_3	$KHCO_3$
(1) 10 cc. potassium caseinate (control) ..	liquid	liquid	liquid
(2) 10 " " " + 0.004 mol. salt	↓		↓
(3) 10 " " " + 0.008 " "			
(4) 10 " " " + 0.012 " "			
(5) 10 " " " + 0.016 " "			
(6) 10 " " " + 0.020 " "		KNO_3 crystals appear	increasing viscosity
(7) 10 " " " + 0.024 " "			gel
(8) 10 " " " + 0.028 " "		↓	salt crystals appear
(9) 10 " " " + 0.032 " "	increasing viscosity		↓ gel
(10) 10 " " " + 0.036 " "	soft gel	solubility of added salt	gel
(11) 10 " " " + 0.050 " "	syneresis	too low to make any increase in viscosity apparent	syneresis
(12) 10 " " " + 0.066 " "	clot and serum		↓
(13) 10 " " " + 0.088 " "	" " "		increasing separation
(14) 10 " " " + 0.100 " "	" " "	↓ increasing deposit of KNO_3 crystals	increasing deposit of ↓ $KHCO_3$ crystals

of colloid changes here being discussed, in the general order monovalent, divalent, trivalent.

The effects of adding a series of different chlorids of the heavier metals to a standard potassium caseinate/water system are shown in Fig. 64 and Table LXXXIII. These experiments may be dismissed with the statement that the effects produced are in all instances dominated by the fact that the basic radical of the added salt reacts with the base of the potassium caseinate to form the corresponding caseinate of the heavier metal. Since these

TABLE LXXXII.—*Potassium caseinate + trisodium citrate*

	Mixture	Remarks
(1)	10 cc. K caseinate (control)	liquid
(2)	10 " " " 0.001 mol. K citrate	increasing viscosity
(3)	10 " " " 0.002 " " "	" "
(4)	10 " " " 0.003 " " "	" "
(5)	10 " " " 0.004 " " "	gel
(6)	10 " " " 0.005 " " "	syneresis
(7)	10 " " " 0.006 " " "	↓
(8)	10 " " " 0.007 " " "	↓
(9)	10 " " " 0.008 " " "	↓
(10)	10 " " " 0.012 " " "	↓
(11)	10 " " " 0.016 " " "	↓
(12)	10 " " " 0.020 " " "	↓
(13)	10 " " " 0.024 " " "	↓
(14)	10 " " " 0.028 " " "	increasing separation

compounds have a lower hydration capacity than the original potassium caseinate (and also a lower solubility in water), the succession of changes previously described is replaced by a simple precipitation of the newly formed less solvatable casein compound. The solvation capacity of the new compound lies, in other words, below the amount of the water present in the total system and so a separation into clot and serum occurs from the moment of first visible change.

3. In order to understand the apparently complicated series of changes that follow addition of an electrolyte to a caseinate/water system it is, in our opinion, only necessary to carry in mind two effects:

TABLE LXXXIII.—*Potassium caseinate + the chlorid of magnesium, strontium, calcium, barium, or iron*

	Mixture	$MgCl_2$	$SrCl_2$	$CaCl_2$	$BaCl_2$	$FeCl_3$
(1)	10 cc. K caseinate + 0.5 cc. H_2O (control)	liquid	liquid	liquid	liquid	liquid
(2)	10 " " " + 0.1 cc. 1/1 m salt sol. + 0.4 cc. H_2O	↓	↓	↓	↓	beginning small tenacious clot
(3)	10 " " " + 0.2 " " " " " " + 0.3 " "	↓	↓	↓	↓	↓
(4)	10 " " " + 0.3 " " " " " " + 0.2 " "	slight increase in viscosity	slight increase in viscosity	↓	↓	↓
(5)	10 " " " + 0.35 " " " " " " + 0.15 " "	↓	↓	↓	↓	↓
(6)	10 " " " + 0.4 " " " " " " + 0.1 " "	↓	↓	increasing cloudiness without apparent increase in viscosity	↓	↓
(7)	10 " " " + 0.5 " " " " " "	increasing amount clear gelatinous precipitate	increasing amount clear gelatinous precipitate	whitish	increasing cloudiness with increasing amount of clot	increasing amount tenacious clot with increasing amount of serum
(8)	10 " " " + 0.3 cc. 2/m salt sol. 0.2 " "			↓		
(9)	10 " " " + 0.35 " " " " " " + 0.15 " "			↓		
(10)	10 " " " + 0.35 " " " " " " + 0.15 " "			↓		
(11)	10 " " " + 0.5 " " " " " "			increasing separation to clot and serum		

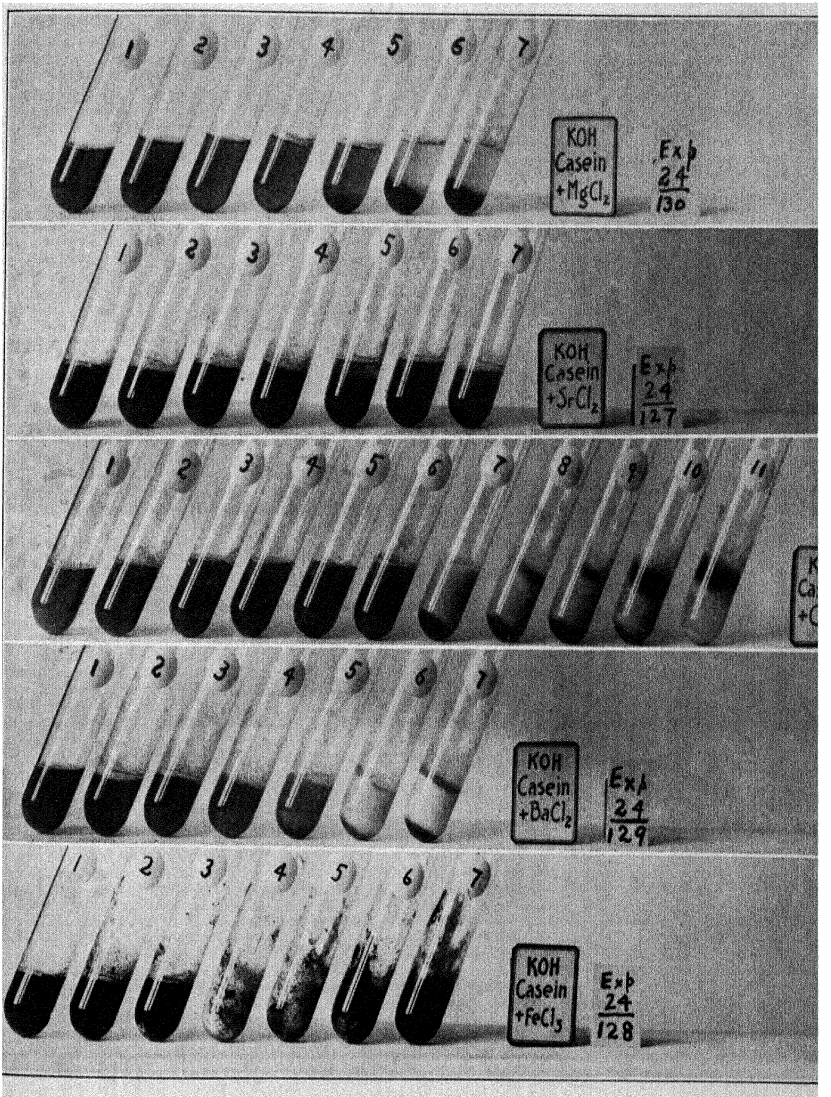

1 2 3 4 5 6 7
KOH Casein +MgCl2
Exp 24 130
1 2 3 4 5 6 7
KOH Casein +SrCl2
Exp 24 127
1 2 3 4 5 6 7 8 9 10 11
1 2 3 4 5 6 7
KOH Casein +BaCl2
Exp 24 129
1 2 3 4 5 6 7
KOH Casein +FeCl3
Exp 24 128

FIG. 64

(a) *An added neutral salt may produce a first change in any given caseinate/water system through reaction with the caseinate itself.* Thus a sulphate added to a casein chlorid will and does form, through double decomposition, at least some casein sulphate; while a barium or calcium salt added to a potassium or sodium caseinate will similarly yield the barium or calcium caseinate. Since the latter compounds have a lower hydration capacity (and also a lower solubility in water) the effect of such addition will, obviously, reduce the viscosity and transparency of the treated caseinate. If the caseinate thus produced through double decomposition has a sufficiently low hydration value it will fall out as a precipitate. The matter is illustrated in Figs. 55 and 65. The entire colloid-chemical behavior from decrease in viscosity to loss of transparency and precipitation is the product of dehydration of the lyophilic colloid, induced in this case by the chemical production of a new caseinate with decreased solvent power *for* water.

(b) *But an added neutral salt may produce a second change in any given caseinate/water system* independently of any such double decomposition. *The addition of a neutral salt incapable of reacting chemically with a caseinate nevertheless brings about a series of changes in the physical state of the total system which may be described as follows: following a first progressive increase in viscosity to a maximum of actual gelation* (if the water concentration is not too high) *there follows a gradual decrease in viscosity with progressive decrease in the volume of the caseinate mass and a squeezing off of "serum" until the caseinate is completely salted out.*

The caseinate is again precipitated because dehydrated but the dehydration is produced not through an effect of the neutral salt upon the colloid primarily but upon the solvent (the water). What happens is analogous to the similar set of physico-chemical changes to be observed in the salting out of a soap (like potassium oleate) by a neutral salt (like potassium chlorid) incapable of reacting chemically with the soap and our explanation for both sets of phenomena is the same.[57] *The salt unites with the solvent.* This "salt water" is then emulsified *within* the hy-

[57] See MARTIN H. FISCHER and MARIAN O. HOOKER: Chemical Engineer, *27*, 223 (1918); Soaps and Proteins, 93 and 114, New York (1921).

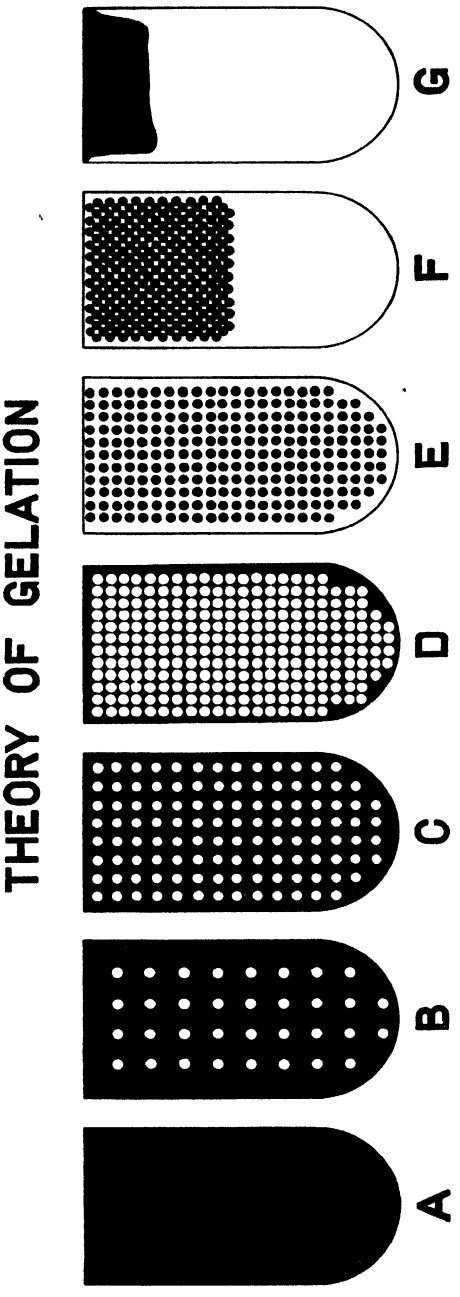


FIG. 65

drated colloid, as shown in diagram B of Fig. 65. Since emulsions are more viscid than the phases which compose them, the result is an increase in the viscosity of the total system. Such increase in viscosity obviously must increase hand in hand with increase in the amount of added salt until a maximum is reached (diagram D) and the "salt water" phase has become so large that it can no longer be enveloped by the hydrated colloid. A change in arrangement of the phases now comes about, and what was an emulsion of salt water in the caseinate changes to one of hydrated caseinate within the salt water (diagram E). The system now begins to "sweat" (shows syneresis) and, upon still further addition of salt, separates into the two gross phases "serum" (salt water) and "clot" (practically dehydrated protein) (diagram G).

4. The addition of increasing amounts (1 to 5 grams) of two sugars (saccharose and dextrose) to a standard potassium caseinate/water system (10 cc.) produces no visible change in viscosity and no precipitation. Weight or molar equivalents of levulose, milk sugar, alcohol and glycerin are similarly ineffective.

This difference between electrolytes and non-electrolytes upon proteins has long been recognized and has usually been ascribed to the differences in the electrical properties of the two types of material when "dissolved in water." In our view, this has little to do with the matter as the experiments on silicic acid systems detailed in the next section will show.

When a salt which does not react chemically with a given proteinate nevertheless dehydrates and precipitates it, this is because the salt unites with the solvent as previously described. To bring about a separation, the proteinate must not be soluble in or solvatable by the "salt water." When sugar or alcohol is used in corresponding concentration, these too unite with the solvent,[58] but the proteinate still remains soluble in and solvatable by such "sugar water," and so the whole system remains clear and does not increase in viscosity nor gel. The matter finds its analogue in the behavior of the soaps towards sugars and the alcohols. From a "solvent" point of view sugar behaves like

[58] Unpublished experiments of JOSEPH L. DONNELLY.

an alcohol and neither material "salts out" a soap, since the soap is solvated by both. In other colloids (like silicic acid or pectin) this tendency to dissolve in or to be solvated by "sugar water" does not occur and the sugars, alcohol, etc., then become as good precipitants as the electrolytes themselves. The next section illustrates such behavior.

B. The System Silicic Acid/Water

Silicate systems were among the first[59] upon which studies were made illustrative of the existence and the nature of "colloids," yet in spite of this fact there is still lacking any generally accepted concept of their true constitution. They are lyophilic colloids, their water content varies under a wide range of circumstances, they yield sols and gels, but why they do this is a matter of debate. The following paragraphs attempt to classify a fraction of the vast number of silicate systems known, albeit one which has received the largest amount of scientific study, namely, that in which (as some hold) the anhydrid of silicic acid (SiO_2) or (as we think more correct) this in one of its several combinations with water (H_4SiO_4, H_2SiO_3 or $H_6Si_2O_7$, $H_4Si_2O_6$, etc.) is made to appear in an aqueous system through decomposition of some soluble silicate, like sodium silicate, by a chemically necessary equivalent of acid. The experiments here detailed are therefore not new in the regions of mere fact but they have been arranged differently in an effort to discover if the definitions and the structures that we have assigned to the lyophilic colloids in general may not find satisfactory application to these specific systems.

Our experiments started with the same ground material, namely, a half molar solution of highly purified sodium silicate ($Na_2SiO_3 \cdot 8H_2O$). The sodium silicate was either bought as such or was prepared by ourselves in half molar strength through addition to each other in the cold of standardized weights of highly purified silicic acid and sodium hydroxid in water. For purposes of control we permitted the sodium silicate prepared by ourselves to crystallize out, subsequently redissolving the crys-

[59] THOMAS GRAHAM: Liebig's Annalen d. Physik, *121*, 36 (1862); J. M. VAN BEMMELEN: Die Absorption, 39, Dresden (1910); E. GRIMAUX: Compt. rend., *98*, 1437 (1884).

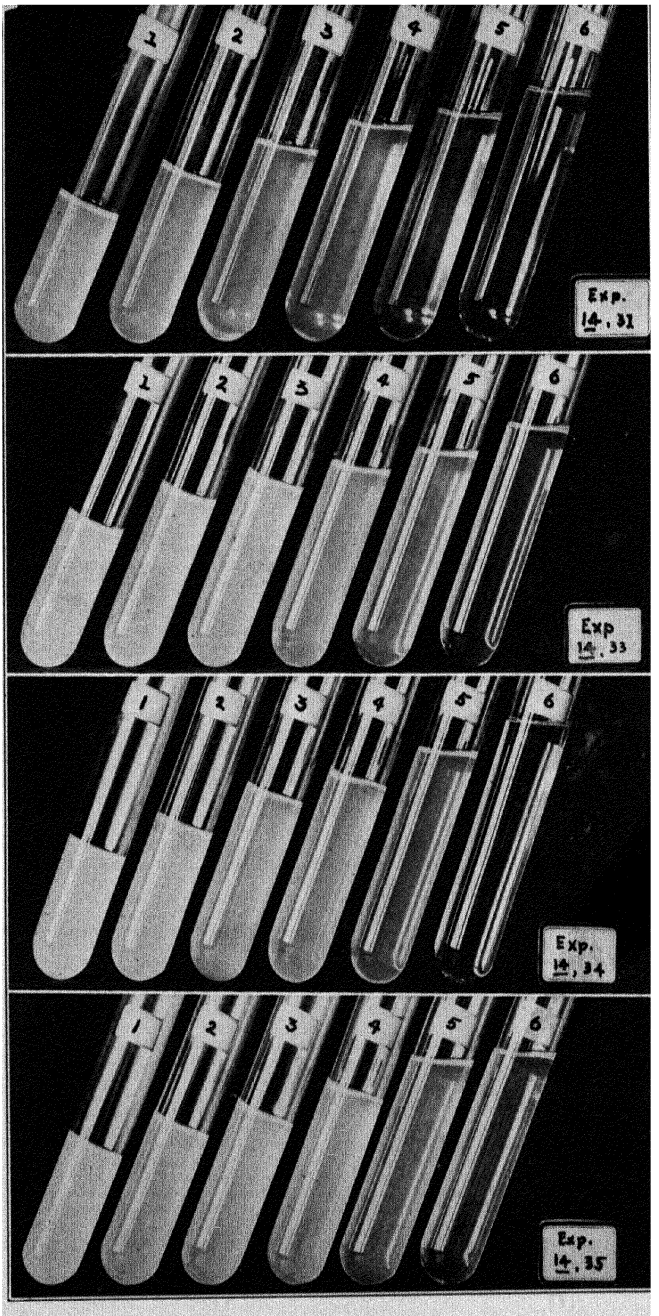


FIG. 66

tals in the necessary amount of water to give us our standard solution.

We found that these solutions of sodium silicate were always clear as water, non-viscid and by themselves free from all "colloid" properties. Moreover, they retained these properties throughout the months that we kept them in well stoppered, hard glass containers. *A pure sodium silicate/water system as thus formed is therefore non-colloid.*[60]

1. We wished first to repeat the old experiment of the production of a colloid silicic acid by neutralizing a standard solution of such sodium silicate with an acid of some sort. The results for four different acids in the order sulphuric, hydrochloric, acetic, lactic are shown in Fig. 66 and Table LXXXIV. It will be noted that in all instances a definite volume of standard sodium silicate was mixed with an amount of normal acid theoretically necessary to produce complete decomposition of the sodium silicate and a setting free of its silicic acid, the variable in the experiment being represented by the progressive increase in amount of water present in the reaction mixture.

Independently of the varying "strength" (hydrogen ion concentration) of the four acids employed, the same effect has been produced throughout, but depending upon the concentration of the water in the system, there has been formed everything from a solid gel in the lowermost concentration of water, through gelatinous and liquid colloid sols in the middle, to a water-clear solution at the extreme right which, so far as ordinary appearances go, looks like a true solution.

If we try to interpret these findings, it is obvious, first, that the hydrogen ion concentration of the acids used was *not* responsible either for the production of the colloid silicic acid or for the colloid properties of the systems finally produced, for while

[60] We emphasize this fact because the ordinary solutions of water-glass, so frequently used in studies of this sort are by themselves distinctly colloid. Such water-glass cannot, therefore, be "pure" sodium silicate. It has colloid properties either (1) because it contains free silicic acid or (2) because it represents a mixture of several sodium silicates. We incline, in other words, to the view of GRIMAUX who believes that SiO_2 can unite chemically with one, two, three, etc., molecules of water to yield a *series* of *different* silicic acids.

the acids varied from the very strong to the very weak the ultimate colloid mixtures were all the same.

Where in the diagrams of Fig. 2 do these various systems find their place? If the silicic acid (or any hydrated form thereof) is assumed to be solid (or crystalline) at the temperatures involved, diagram B is to be considered. The right hand, fluid tubes of Fig. 66 (those containing the largest volumes of water) are obviously approximations at least, to true solutions which as such belong little below the level A. As the volume of water falls and the mixture shows opalescence, particles of hydrated silicic acid in ever increasing number or size must appear in dispersed form in what remains of the "true" solution of silicic acid in water and the regions B, C and D be reached. The increasing opalescence with increasing viscosity upon further reduction in volume of "solvent" represents some region like E. A definite setting occurs at F where the hydrated silicic acid particles begin to touch each other; and the gel is "dry" anywhere below the level W (anywhere below a level where the hydrated silicic acid forms a continuous external enveloping phase for whatever may remain of a "true" solution of silicic acid in water contained within). When little enough water is present in the system the lowermost level (Z) consisting entirely of a solution of the water in the silicic acid is realized.

In the reaction mixtures represented in Fig. 66 and Table LXXXIV, sodium chlorid is present. It is therefore necessary to compare the observations just described with those appearing in similar mixtures when sodium chlorid is absent. As is well known, the sodium chlorid may be removed in a few days from these mixtures by dialysis against distilled water.

Such dialyzed silicic acid systems are generally said to set much more slowly; it is more correct to say that at these concentrations of water they *will not set at all. But if the amount of water in the various systems is reduced* (by three-quarters, roughly) *the entire set of colloid systems from gel to* (*approximately*) *pure solution of the silicic acid in water can again be obtained.* The systems containing sodium chlorid set faster and better simply because the salt combines with the water and so reduces the total amount of solvent present, as will be discussed in the next paragraphs. We have kept properly prepared and

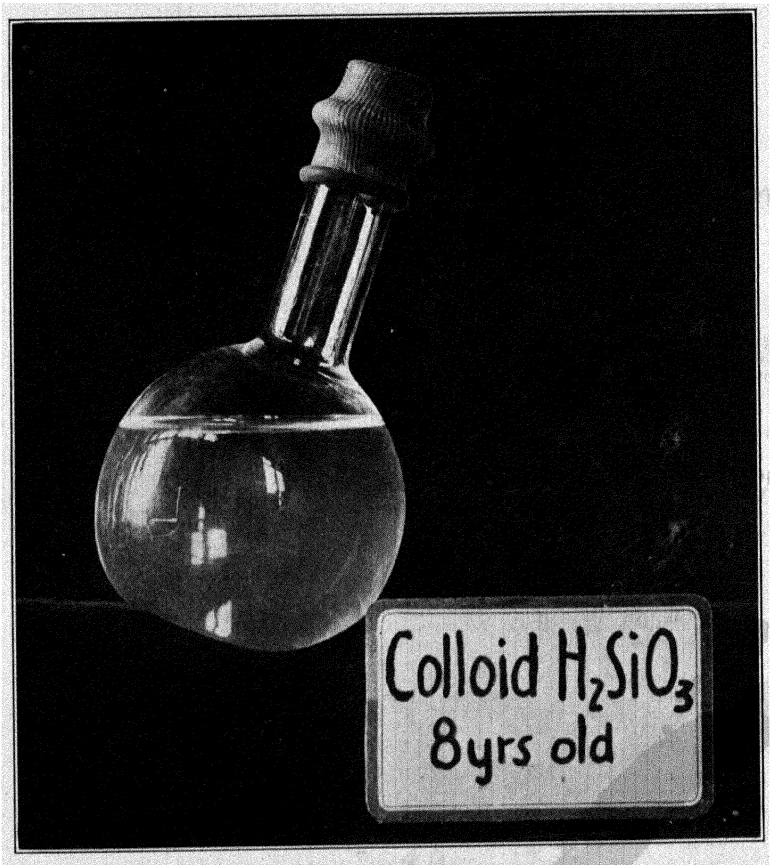


FIG. 67

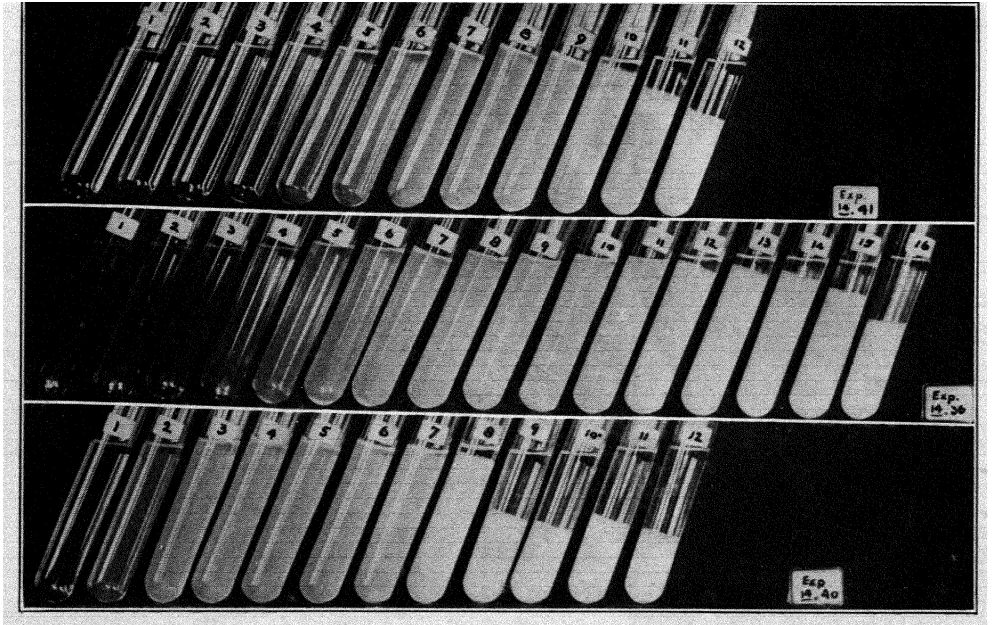


FIG. 68

purified (and sufficiently dilute) colloid silicic acid sols in unchanged form for years. Fig. 67 is a proof of this. The (hard glass) flask contains a barely opalescent, water-like, colloid silicic acid (in 1/4 n concentration) which has undergone no visible change in nine years. GRAHAM, VAN BEMMELEN and GRIMAUX with many workers since have maintained that such systems do set after weeks or months. Such observations have given rise to the general notion that colloids suffer change "spontaneously" in the process of aging. We think it better to deny the existence of such "spontaneous" change and to believe with these first workers that the presence of salts not removed by dialysis

TABLE LXXXIV.—*Effect of water concentration on sodium silicate/acid systems* (Sulphuric, Hydrochloric, Acetic, Lactic Acids)

	Concentration of mixture				Appearance after 2–10 days
(1)	5 cc. 1/2 m Na_2SiO_3	+ 5 cc. H_2O	+ 5 cc. n acid		solid, dry gel
(2)	5 cc. " " "	+ 7.5 cc. "	+ 5 cc. " "		" " "
(3)	5 cc. " " "	+ 10 cc. "	+ 5 cc. " "		" " "
(4)	5 cc. " " "	+ 12.5 cc. "	+ 5 cc. " "		viscid gel
(5)	5 cc. " " "	+ 15 cc. "	+ 5 cc. " "		viscid sol
(6)	5 cc. " " "	+ 17.5 cc. "	+ 5 cc. " "		opalescent sol
(7)	5 cc. " " "	+ 20 cc. "	+ 5 cc. " "		barely opalescent
(8)	5 cc. " " "	+ 22.5 cc. "	+ 5 cc. " "		non-viscid, clear as water
(9)	5 cc. " " "	+ 25 cc. "	+ 5 cc. " "		" " " " "
(10)	5 cc. " " "	+ 30 cc. "	+ 5 cc. " "		" " " " "

or traces derived from the containers or through air contamination of imperfectly protected mixtures are really active and in the manner now to be discussed.

2. In Fig. 68 and Table LXXXV are shown the effects of the addition in increasing concentrations of three chlorids (lithium, sodium and potassium) to such a silicic acid/water system as was found in Fig. 66 and Table LXXXIV *not* to yield a system showing any definite colloid properties in weeks or months. The mixture had the concentration values shown in the first line of Table LXXXV. As Fig. 68 shows, other conditions being the same, the addition of any of these salts in increasing concentration to such a mixture leads, first, to an opalescence and increase in the viscosity of the system until a solid gel is formed beyond which

TABLE LXXXV.—*Effect of neutral salt concentration on sodium silicate/acid systems*
(Lithium chlorid, Sodium chlorid, Potassium chlorid*)

	Concentration of mixture	Appearance of the NaCl series after 2–10 days
(1)	5 cc. 1/2 m Na_2SiO_3 + 20 cc. H_2O + 5 cc. n HCl (control)	barely opalescent liquid
(2)	5 cc. 1/2 m Na_2SiO_3 + 19.8 cc. H_2O + 0.2 cc. 5/m salt + 5 cc. n HCl	
(3)	5 cc. " " " + 19.6 cc. " + 0.4 cc. " " + 5 cc. " "	
(4)	5 cc. " " " + 19.4 cc. " + 0.6 cc. " " + 5 cc. " "	
(5)	5 cc. " " " + 19.2 cc. " + 0.8 cc. " " + 5 cc. " "	
(6)	5 cc. " " " + 19 cc. " + 1 cc. " " + 5 cc. " "	increasingly viscid, increasingly turbid sols
(7)	5 cc. " " " + 17.5 cc. " + 2.5 cc. " " + 5 cc. " "	gel
(8)	5 cc. " " " + 15 cc. " + 5 cc. " " + 5 cc. " "	gel with beginning syneresis
(9)	5 cc. " " " + 12.5 cc. " + 7.5 cc. " " + 5 cc. " "	
(10)	5 cc. " " " + 10 cc. " + 10 cc. " " + 5 cc. " "	
(11)	5 cc. " " " + 7.5 cc. " + 12.5 cc. " " + 5 cc. " "	increasingly opaque and less viscid
(12)	5 cc. " " " + 5 cc. " + 15 cc. " " + 5 cc. " "	separation of clot and serum
(13)	5 cc. " " " + 2.5 cc. " + 17.5 cc. " " + 5 cc. " "	
(14)	5 cc. " " " + 20 cc. 5/m salt + 5 cc. n HCl	
(15)	5 cc. " " " + 24 cc. 5/m salt + 1.5 gms. dry salt + 1 cc. 5/n HCl	
(16)	5 cc. " " " + 24 cc. " " + 3 " " " + 1 cc. " "	increasing separation

* A 4/m potassium chlorid solution was used, proper correction of course being made in the amount of water added to the systems.

there occurs a softening which increases until an ultimate coarse separation of the silicic acid from the aqueous dispersion medium is obtained.

How may these successive changes be understood? Clearly, when a salt, like sodium chlorid, is added to the mixture under discussion the possibilities for chemical reaction between the various dissolved substances are practically nil. The sodium chlorid does not, in other words, produce any new compounds. But even when lithium chlorid or potassium chlorid are used, practically identical effects are obtained both qualitatively and quantitatively.

Such light metal salt effects are commonly held to be due to "adsorption" of the salts or their ions by the silicic acid or to the neutralization of its electric charges. These explanations have many weaknesses of their own but they also do nothing to make clear why the silicic acid so frequently gels before being precipitated, or the relationship of the gelling process to the precipitation of the silicic acid.

Our explanation of what happens in the case of soap/water and protein/water systems applies to these silicic acid/water systems when treated with a chemically neutral and non-reacting salt. The sodium chlorid (or other salt) added to the silicic acid/water system again unites with the water; and the salt-water thus formed is then "emulsified"[61] in the remaining portions of the system. The first effect of the addition of the salt is, obviously, to deprive the system of a part of the solvent. This represents, therefore, conversely stated, an increase in the concentration of the silicic acid in the remaining portion of the system. With the first portions of salt added, the salt-water formed is emulsified within the silicic acid-water phase. Because of the double effects of the increase in the concentration of the silicic acid and that of the emulsification of the one material within a second there follows opalescence with increase in viscosity up to a point where actual gelation occurs (B, C, D of Fig. 65). With still further increase in the concentration of the salt, the salt-

[61] Emulsions are by definition subdivisions of a liquid in a liquid. The term "emulsification" is therefore a poor one to use when one of the phases, as in silicic acid systems, is assumed to be solid, but we know of no better way of expressing our meaning.

water phase becomes so large in amount as to become the external enveloping phase for the hydrated silicic acid phase. In other words, the emulsion changes to one of opposite type. The transition point is shown diagrammatically in E of Fig. 65 and is represented in the actual experiments by the syneresis and secondary liquefaction which follows the gelation in the silicic acid/water/salt systems. Further addition of salt increasingly dehydrates the silicic acid (F, G of Fig. 65) until it separates in coarse form from the dispersion medium, and falls as the precipitate observable in the end tubes of Fig. 68.

When the gelation and precipitation effects of the several chlorids are compared with each other they are found to be about equal. If our experiments and our explanation may be trusted, it would therefore seem that the molar dehydration effects of these three salts is practically the same.

3. We studied next the gelation and precipitation effects of a series of salts with a common base but different acid radicals. The results with various sodium salts in the order chlorid, bromid, iodid, silicate, acetate and sulphate are illustrated in Fig. 69 and Table LXXXVI. The colloid changes induced are qualitatively and quantitatively identical. When the different salts are added at the same molar concentration to a silicic acid/water system which by itself does not gel there is, with increasing concentration of the added salt, a gradual development of opalescence with increase in viscosity to a point where the whole mixture sets into a solid jelly. Only the changes up to this point are shown in Fig. 69 and Table LXXXVI but wherever the solubility of the employed salt permitted of it, its further addition brought about syneresis, a secondary liquefaction and separation of the silicic acid in coarse form from the dispersion medium.

We explain these changes also through union of the added salts with the water followed by an increase in the concentration of the silicic acid in the remaining water and the effects of the emulsification of the one phase in the second, as already described.

4. In order to buttress the notion that it is not primarily any action of the added salts upon the silicic acid which is responsible for the colloid changes just described and also to indicate that it is not any electric charge effect that is most significant

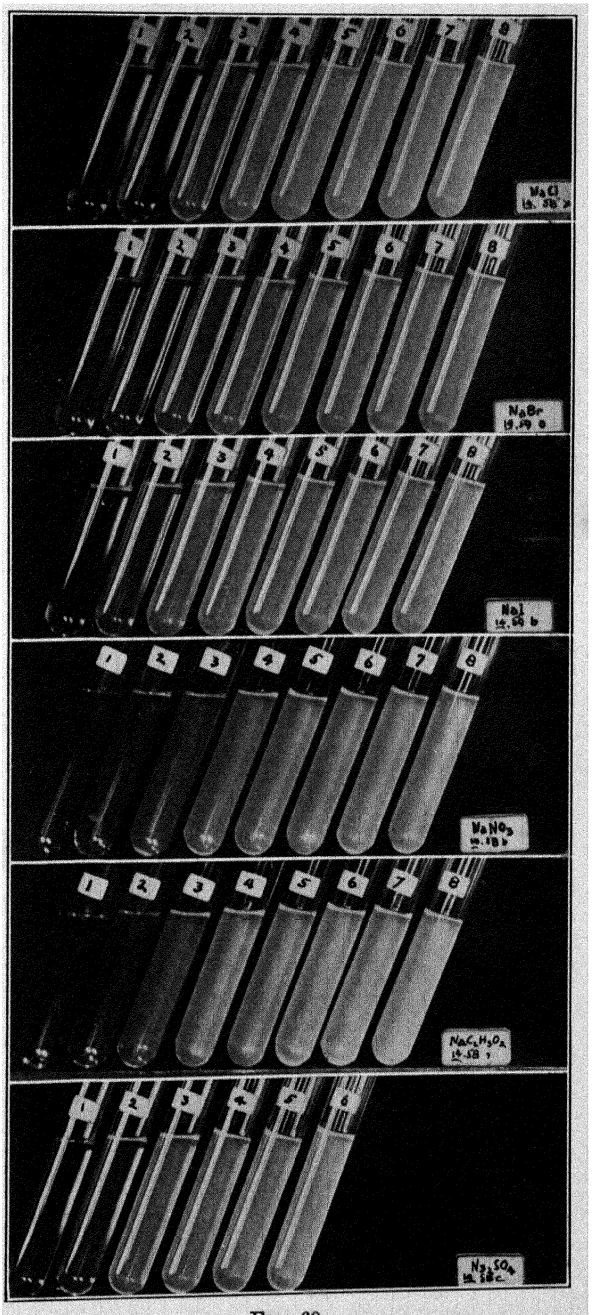

1 2 3 4 5 6 7 8
NaCl
1 2 3 4 5 6 7 8
NaBr
1 2 3 4 5 6 7 8
NaI
1 2 3 4 5 6 7 8
NaNO3
1 2 3 4 5 6 7 8
NaC2H3O2
1 2 3 4 5 6
Na2SO4

FIG. 69

TABLE LXXXVI.—*Effect of sodium salts with different acid radicals on sodium silicate/acid systems*
(Sodium chlorid, bromid, iodid, nitrate, acetate and sulphate*)

	Concentration of mixture	Appearance after 2–10 days
(1)	5 cc. 1/2 m Na_2SiO_3 + 20 cc. H_2O + 5 cc n HCl	barely opalescent liquid
(2)	5 cc. 1/2 m Na_2SiO_3 + 19 cc. H_2O + 1 cc. m salt + 5 cc. n HCl	
(3)	5 cc. " " " + 18 cc. " + 2 cc. " " + 5 cc. " "	
(4)	5 cc. " " " + 17 cc. " + 3 cc. " " + 5 cc. " "	
(5)	5 cc. " " " + 16 cc. " + 4 cc. " " + 5 cc. " "	
(6)	5 cc. " " " + 15 cc. " + 5 cc. " " + 5 cc. " "	increasingly opalescent and increasingly viscid sols
(7)	5 cc. " " " + 12.5 cc. " + 7.5 cc. " " + 5 cc. " "	gel
(8)	5 cc. " " " + 10 cc. " + 10 cc. " " + 5 cc. " "	gel

* Because of its limited solubility a 1/4 m solution of this salt was used.

TABLE LXXXVII.—*Effect of different alcohols on sodium silicate/acid systems*
(Monatomic: Methyl, ethyl, propyl, iso-butyl)
(Diatomic: Trimethyleneglycol)
(Triatomic: Glycerin)

Concentration of mixture	Appearance after 2–10 days
(1) 5 cc. 1/2 m Na_2SiO_3 + 20 cc. H_2O + 5 cc. 1/1 n HCl	barely opalescent liquid
(2) 5 cc. 1/2 m Na_2SiO_3 + 19 cc. H_2O + 1 cc. alcohol (absolute) + 5 cc. n HCl	
(3) 5 cc. " " " + 18 cc. " + 2 cc. " " + 5 cc. " "	
(4) 5 cc. " " " + 17 cc. " + 3 cc. " " + 5 cc. " "	
(5) 5 cc. " " " + 16 cc. " + 4 cc. " " + 5 cc. " "	
(6) 5 cc. " " " + 15 cc. " + 5 cc. " " + 5 cc. " "	increasingly opalescent and
(7) 5 cc. " " " + 12.5 cc. " + 7.5 cc. " " + 5 cc. " "	increasingly viscid sols
(8) 5 cc. " " " + 10 cc. " + 10 cc. " " + 5 cc. " "	gel
(9) 5 cc. " " " + 7.5 cc. " + 12.5 cc. " " + 5 cc. " "	gel
(10) 5 cc. " " " + 5 cc. " + 15 cc. " " + 5 cc. " "	gel

C. The System Heavy Metal Soap/X[61]

As further proof that it is a mutual solubility of the phases (and not some restricted and accidental factor like the presence or absence of certain ions) which gives the lyophilic colloids their various and varying characteristics, we introduce the following observations on colloid systems in which such secondary factors disappear.

Fig. 71 is introduced for purposes of orientation only. It shows the well known behavior of gutta percha when standard cubes weighing one gram each are left to themselves for several days at room temperature in 50 cc. of various solvents, they being from left to right, in the illustration, water, absolute ethyl alcohol, paraffin oil, linseed oil, anilin, pyridin, ethyl ether, carbon tetrachlorid, chloroform, toluene, xylene, benzene. No swelling is observable in water or alcohol. From here on, there is increase in the amount of swelling (eye measure only, since the mass of rubber becomes too soft to weigh) in the order given. There is little possibility, obviously, of finding in these different systems any electrical factors to account for their swelling, their "peptisation," their "solution," or any other attribute of a lyophilic colloid system.

Large numbers of other systems are known to the colloid chemist which behave in identical fashion and in which no electrical properties of any kind are apparent to explain their behavior, as witness the carbohydrate gums with water, various lipoids with water, nitrocellulose with alcohol-ether, nitrocellulose with anhydrous acids, cerotic acid with anhydrous alcohol, etc. What is common to all these systems is a well marked (medium!) degree of mutual solubility.

In the following paragraphs are detailed a series of quantitative observations on some typical lyophilic colloid systems in which electrical properties are again conspicuously absent, but in which the factor of mutual solubility is universal. They concern themselves with various soaps of the heavier metals and various organic solvents and as such extend our earlier observations on the soaps.

[61] MARTIN H. FISCHER and MARIAN O. HOOKER: Kolloid-Zeitschrift, *51*, 39 (1930).

The soaps of the lighter metals are "electrolytes," but that this is not the factor which determines their colloid behavior is already proved by the fact that those which are weakest as electrolytes (the soaps of the higher fatty acids for example as opposed to those of the lower) yield the best and most stabile of lyophilic colloids; and all of them are stabilized and solvated, for example, as greatly (or more greatly) by various alcohols as by water. And this stabilization and solvation are still clearly evident when in place of some alcohol, various hydrocarbons, various wood distillates, various ethers or various aldehydes are employed.[62]

We pass now to the consideration of systems composed of some soaps of the heavier metals with such non-aqueous "solvents."

The different heavy metal soaps used in the following experiments were all prepared in identical fashion, through double decomposition of a potassium soap with a chemically equivalent amount of the necessary heavy metal salt. The potassium soap was used in half molar concentration; the decomposition salt, as a solution of equivalent concentration, being employed always in slight excess. The soap was poured into the solution of the heavy metal salt. Usually the chlorids of the heavy metals were used; but in the case of the weaker metallic bases, the acetates. The precipitated soaps were allowed to stand 24 hours, filtered and washed quickly with several changes of distilled water until practically free of adherent salts, care being taken not to press such washing to the point of obtaining hydrolysis of the heavy metal soaps.

It should be noted that the metallic soaps thus prepared are *not* absolutely pure,[63] but uniformity in the scheme of their preparation makes the error inherent in their production fairly uniform throughout. The washed soaps were reduced to an anhydrous condition by careful heating in an oven, the temperature not being pushed beyond 100°, until the soap was practically dry.

[62] MARTIN H. FISCHER and MARIAN O. HOOKER: Chemical Engineer *27*, 184 (1919); Soaps and Proteins, 60, New York (1921).

[63] MARTIN H. FISCHER and MARIAN O. HOOKER: Soaps and Proteins, 9, New York (1921).

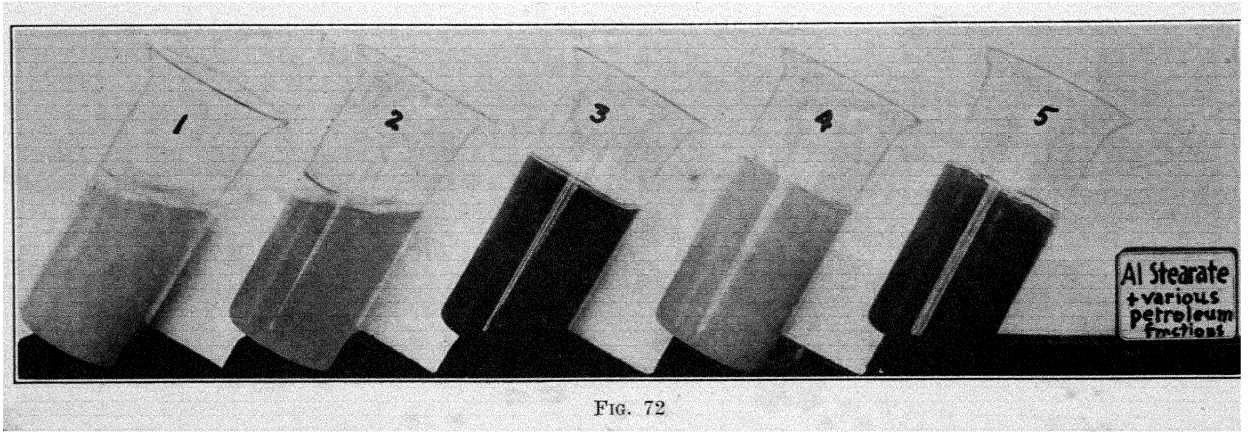


FIG. 72

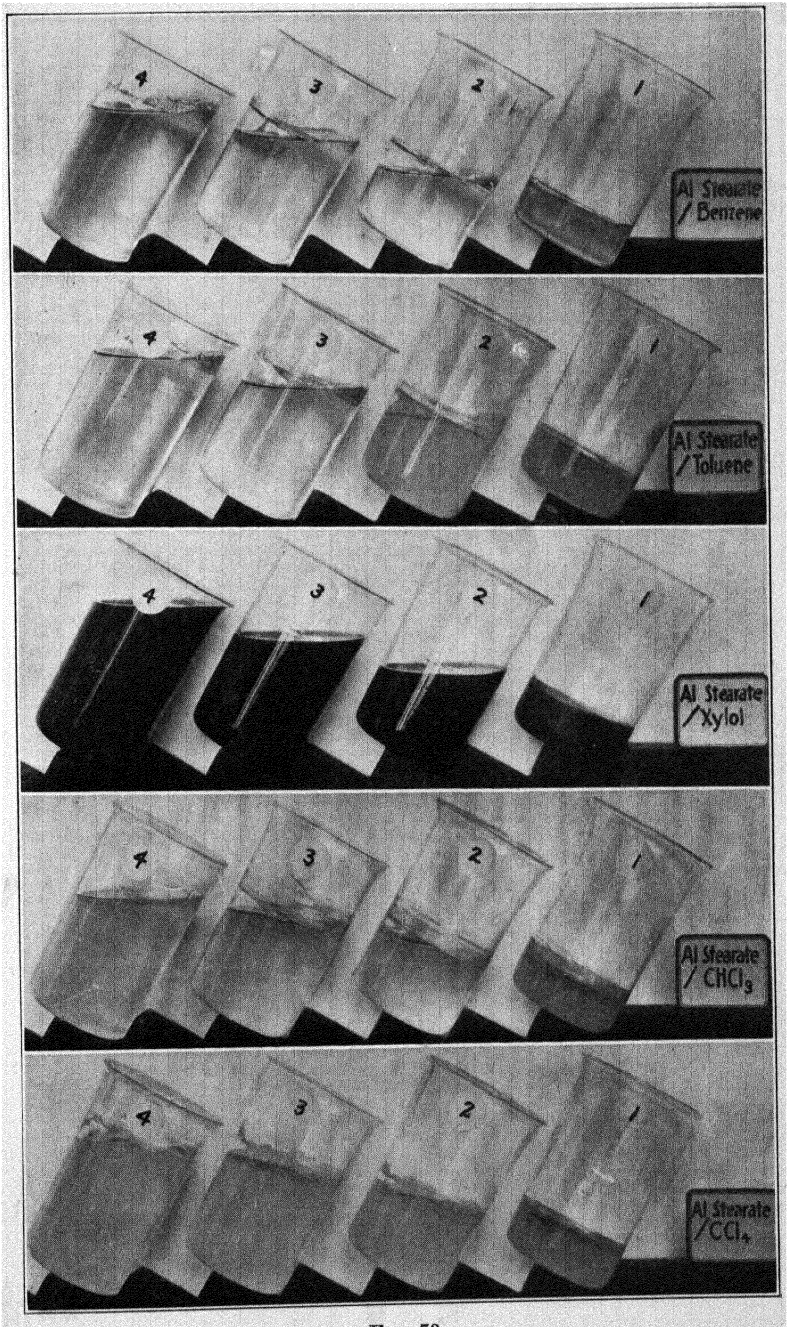

4
3
2
1
Al Stearate / Benzene
4
3
2
1
Al Stearate / Toluene
4
3
2
1
Al Stearate / Xyloi
4
3
2
1
Al Stearate / $CHCl_3$
4
3
2
1
Al Stearate / CCl_4

FIG. 73

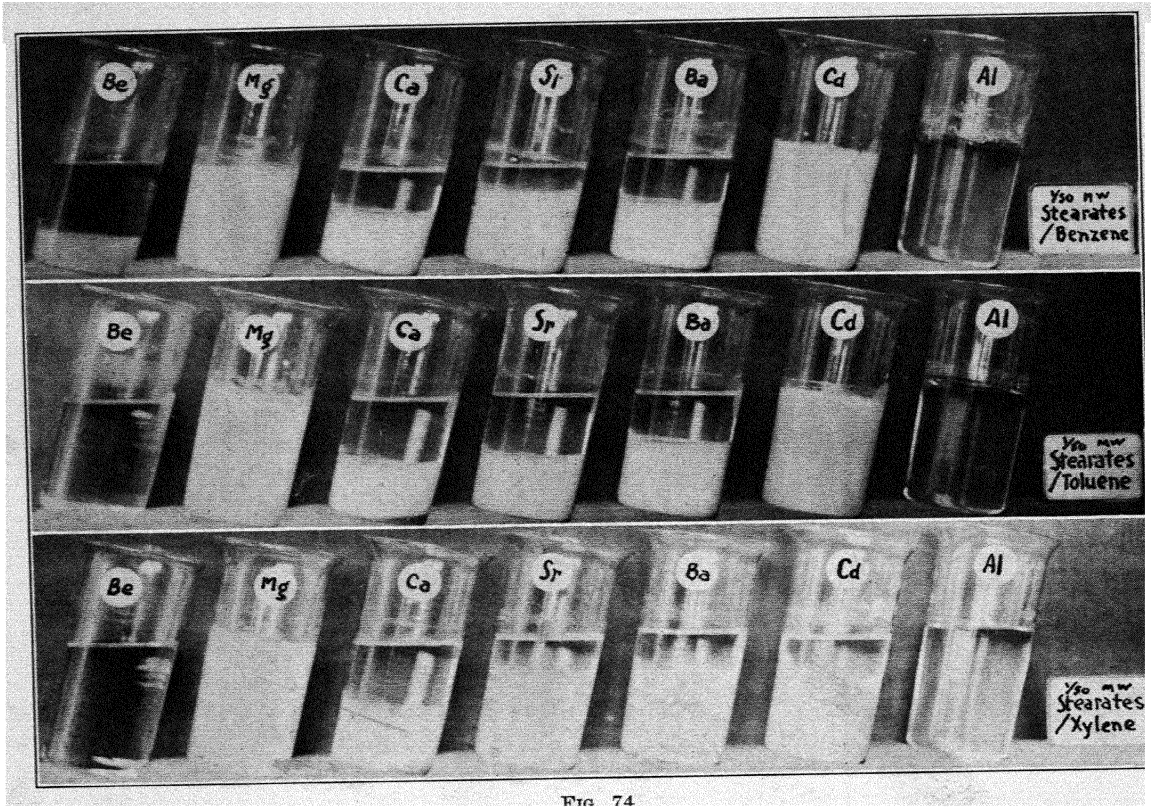

Be
Mg
Ca
Sr
Ba
Cd
Al
1/50 M.W. Stearates / Benzene
1/50 M.W. Stearates / Toluene
1/50 M.W. Stearates / Xylene

FIG. 74

chemically purer organic solvents (benzene, toluene, xylene, chloroform and carbon tetrachlorid). "Solution" was brought about as before. It should be noted that, even in the cold, the metal soap again "swelled" in these different "solvents," as so much gelatin in water. When heated, it went into clear solution. On cooling, *glass-like* colloid solutions or gels were obtained, depending upon the quantity of solvent originally mixed with the soap. When much such solvent was used, the viscid, water-clear mixtures shown in the beakers marked 4 were obtained. With less of the "solvent," increasingly viscid but still water-clear soft gels were formed which in the highest concentration of the soap yielded the solid gels shown in the beakers marked 1.

We see in the four different members of the different series the several colloid systems previously enumerated, beginning with a sol (the dispersion of solvated soap particles in a solution of the soap) and ending with the solid gel (in essence a (solid) solution of the solvent in the soap.)

Fig. 74 illustrates what happens when some other base takes the place of aluminium in a stearate in the case of the three "solvents" benzene, toluene and xylene. We deal, from left to right, with the stearates of glucinum, magnesium, calcium, strontium, barium, cadmium and aluminium. Molar equivalents (1/50 gram mol.) were again dissolved, as before, in 100 cc. of the different solvents.

The aluminium stearate again yielded a glass-like solid gel, as shown in the seventh beakers on the extreme right. The gelation capacity for magnesium and cadmium stearates was equally great, though the gels were white (second and sixth beakers). Glucinum stearate, on cooling, fell out as a gelatinous precipitate but less in amount in the three solvents in the order benzene, toluene, xylene. Calcium, strontium and barium stearates also yielded, at this relative concentration of soap to solvent, only heavily solvated precipitates, with the amount of such precipitate increasing in the order benzene, toluene, xylene. With less "solvent" present, these soaps yielded white gels.

Study of these various systems indicates therefore that while all these soaps yield gels with these solvents, aluminium stearate has the greatest capacity in this regard. Of the alkaline earth bases, magnesium has the greatest capacity, with barium, stron-

tium and calcium following in about the order named. There would seem to exist a relation between these elements as associated in the periodic system and this ability to yield gels. But such relation falls off markedly or disappears when other metal soaps are compared. If magnesium is placed in a class with cadmium, both are seen to be good gel producers; but zinc and mercury stearate, while they go into clear solution in these solvents at a higher temperature, fall out on cooling, in practically unsolvated form. Both tin and lead stearate show a very low gel producing capacity, and copper, practically none. This is also true of titanium. Bismuth stearate falls out as a gelatinous precipitate. Thallium stearate, on the other hand, has a high gel producing capacity; at the same molar concentration it is fully as effective as aluminium, though the resulting gels are more definitely crystalline and deeply opalescent or white.

Fig. 75 shows how the gel producing capacity of a heavy metal soap increases with the complexity of its fatty acid. Molar equivalents (1/50 gram mol.) of the laurate, myristate, palmitate and stearate of aluminium were mixed with 100 cc. of five different solvents, benzene, toluene, xylene, chloroform, carbon tetrachlorid. All were treated in identical fashion. It will be noted that water-clear gels were formed in all cases except in the instances of the palmitate and stearate with chloroform and carbon tetrachlorid, with which "solvents" opalescent gels resulted. The gels were increasingly firm in each series, in the direction laurate to stearate.

The sheer beauty of these gels is worthy of note. But we believe that optically clear systems of this kind require a scientific thought and analysis which if allowed them will do much to clarify the confusion now existing regarding the essential nature of lyophilic colloid systems and of "true" solutions as the chemist views them. No one, of course, doubts the lyophilic colloid nature of the systems here under discussion. We know from their position in series experiments that they are in our terminology "solutions" of the solvent in these soaps. But we feel confident that many a "solution" of this type has been classified by the chemist working on "solubility" (in the sense of molecular solubility of x in the solvent) as a true solution. With a

little more of the "solvent" added to these gels they remain sols and physico-chemical measurements then show the total systems to be dominated by the characteristics of the ordinary "dilute" solution. Small wonder that the physical chemists have found the mathematical formulae derived from study of the dilute solutions to be applicable to all such colloid systems if only a factor or two is allowed them.[65] And yet because the solution of x in the solvent passes over to an optically indistinguishable solution of the solvent in x we have never been clear ourselves in systems involving these solvated colloids when "solution" in the orthodox chemist's sense of the word had occurred.

Comparison of any soap of the acetic series with one of the oleic always showed the latter to be a poorer gel producer. While various metal oleates, for example, increased the viscosity of any hydrocarbon to which they were added, they proved themselves incomparably less effective in this regard than the corresponding stearates.

The following may be stated regarding the formation of gels from metal soaps and solvents not already enumerated. Unless otherwise noted, 1/50 gram mol. of the heavy metal soap was mixed with 100 cc. of the organic solvent. Aluminium stearate yielded a good gel with ethylene chlorid and with hexane, heptane and decane; but aluminium stearate, palmitate, myristate or laurate did *not* yield gels with pentane; nor did aluminium stearate yield a gel with anilin, pyridin, cresol, orthotoluidin, or benzyl benzoate. Lead palmitate yielded a solvated precipitate on cooling from solution in benzene.

Fig. 76 illustrates, in the instance of cadmium stearate (3.39 gm.) with toluene (50 cc.), a phenomenon common to many of these heavy metal soap/organic solvent systems and one which we deem of great theoretical importance in the interpretation of colloid behavior. At a high temperature (100°), the soap dissolves in the organic solvent to yield a clear molecular solution (first beaker on the left). When the temperature is permitted to fall (60°), a thick gel reminiscent of egg-white is produced (middle beaker); but if the temperature is dropped still further (6°), crystallization occurs (as shown in the beaker on the right)

[65] See page 173.

with separation of a fluid phase (syneresis). The process is reversible. The same series of changes may be observed in the case of strontium stearate/toluene, and aluminium stearate/benzene, /pyridin, or /ethylene chlorid.

The phenomenon is of interest as going against the ordinary rule that a solvated colloid with falling temperature becomes increasingly solvated and increasingly viscid or solid. To explain the matter, we have to say that in the middle regions of temperature we deal with liquid/liquid colloid systems in OSTWALD's terminology which change to (syneretic) solid/liquid mixtures at the lower temperature. The recession in viscosity may then mean that a viscid emulsion has given way to a less viscid solid/liquid system. But something more may also have happened—*the degree of solvation may be greater for the "colloid" when in a liquid state than when in a solid.* Put another way, the "affinity" between solvent and colloid particles is greatest at the higher temperature; that of the solvent particles for each other or the colloid particles for each other (as opposed to that of the colloid particles for the solvent), greatest at the lower temperature.

PART TWO

CHEMICAL APPLICATIONS

PART TWO

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I. The Place of the Lyophilic Colloid System in Chemistry

Even though chemistry is well aware that an enormous number of its apparently homogeneous systems are not such, it continues to work with them as though they were. In this way chemistry has tried—and still tries—to apply the laws of homogeneous equilibrium to systems frankly heterogeneous. In practice the laws are found not to fit, but the attempt to apply them continues nevertheless.

A first corollary to be drawn from the experimental studies detailed in the preceding pages is that a large set of systems—apparently homogeneous—is really heterogeneous. *Many reaction mixtures, when not actually regarded as true solutions, are still approached from this point of view. It would be a step forward if their heterogeneity were recognized and if in their future chemical study they were classed among the lyophilic colloid systems.* We refer to those industrially important groups that appear in the manufacture of soap and various cosmetics, rubber manufacture, the preparation of nitrocellulose derivatives and their manifold employment in the arts, dye-vat chemistry, the whole process of tanning from preparation of the skins to their fixation by tannin compounds or chromium, the manufacture of greases, the manufacture of glues and sizes and the chemical processing of all types of proteins and carbohydrates as seen in the textile industry. Colloid chemists have often enough emphasized the colloid nature of such systems and their lyophilic type; and many a pure chemist has been willing to yield the point. But the necessary consequences of such a decision have not been adopted. It is to these that we need to revert. Nothing for example has arrested the majority of pure chemists and physical chemists from attempting the analysis of their frankly lyophilic colloid systems by purely physicochemical methods.

We hold that the pure chemist and the physical chemist still too largely regard the systems here referred to as mere continua-

tions of their dilute solutions; they may admit that the solutions are "concentrated," but they hold their internal arrangement still to be that of the orthodox solution. For this reason it is well to emphasize that *no such concept (even in the case of the admittedly "colloid" solutions) carries a chemist below the level E of Fig. 2* (that is to say below any level in which the "dissolved" material x is not dispersed (ionically, molecularly or colloidally) *within* the solvent).

Below this level lies a group of dispersoids of inverse type. What requires emphasis is not merely the fact that these dispersoids exist, but that many of those mixtures which the chemist has never believed to lie in this region or to be of such structure are of this nature (like many of his "concentrated" solutions and, of course, all those mixtures which he will accept as being of the lyophilic colloid type). Acceptance of the existence of such dispersoids of inverse type and acceptance of their structure as here outlined necessitates, however, a complete change in point of view regarding what constitutes proper procedure in their analysis. Dispersoids lying above the level E of Fig. 2 carry as an external phase what is in essence a dilute solution and so it is no surprise (as the physical chemists have found) that these total systems show the characteristic of and "behave" predominantly like ordinary dilute solutions; dispersoids lying below this level carry solvated colloid as the external phase, wherefore the total systems no longer exhibit the earmarks of the dilute solution but those of what have here been called solutions of inverse type or solvates. The transition from the one to the other makes for that abrupt change in behavior which, when the physical chemist has not merely ignored it, has been his dismay. It has, on the other hand, yielded the colloid chemist those divergent and new "properties" which have made even the modern disciples of GRAHAM believe themselves at work in "a new world of matter."

The laws of the dilute solution chemist do not apply to his "concentrated" systems nor do they apply to such as we have called solutions of inverse type. The mere introduction of factors into the equations covering the behavior of the dilute solutions is not enough to make them fit the behavior of these dis-

persoids of inverse type. (One observer insists that five constants are called for.) *A new set of laws derived from study of a new type of solution is what is required.*

A study of the diagrams of Fig. 2 will explain why there has been a "debate" in chemistry which has lasted for years. While one side has maintained that colloid systems are "nothing but" true solutions and that a knowledge of such will, by corollary, "explain" everything that happens in any colloid mixture, the other has espoused the view that these colloid systems are something "totally different."

It is obvious that if a horizontal cut is made across any $a + b$ system, say at the level A of Fig. 2, examination of the system will reveal the existence of all the properties of any ordinary dilute solution (a boiling point but little removed from that normal for the solvent, a viscosity roughly that of the solvent, an electrical conductance dependent upon the ions in solution, a C_H or *p*H of a definite value, etc.). *What is more important is that examination of the same a + b system by identical methods at any one of the several lower levels like B, C, D, or E will yield entirely similar physico-chemical findings* and this in spite of the fact that the total system has increased in viscosity, become opalescent, and in other ways betrayed itself as a typical colloid (sol). The explanation is written in the fact that the phase *x*-dissolved-in-the-solvent is still the external phase and that the properties of this external phase are still those most easily discovered as the properties of the total system. Where the physical chemists, who are chiefly responsible for such studies, err, is in their deduction that it is the properties of this one phase which are responsible for what is happening in the other, or in the total system. (They would not otherwise speak of the relation of ionic charge, *p*H, osmotic pressure, etc., to "colloidality," viscosity, gelation, etc.) *It is the other way about.* The fact that more solvent is present at any of the levels so far discussed than can be taken up by the solvatable phase (or as we have called it here, can be "dissolved" or "bound" by it) allows some of the solvated phase to dissolve *in* this excess of solvent. And in this proportion "dilute solution" appears in the total system. But it is not the electrical properties or the *p*H or the osmotic

pressure of this phase which give character to or account for the "behavior" of the total system or of that fraction of it which may be admitted to be "colloid." It depends upon the chemical character of the "colloid," for example, and the quantity of solvent present as to whether *any* dilute solution will at all appear in the total system; and upon the nature of the colloid and the nature of the solvent whether the total system or any part of it will turn out to be a conductor of electricity or not, or show an excess of H or OH ions, etc. A light metal soap or an acid- or base-proteinate with water, for example, will exhibit any "colloid" characteristic we may choose (like a "viscosity" from that of a solid down to that of water) and this independently of any isoelectric point or any specific C_H or pH value. This is because viscosity is a measure of the number and the size of the solvated soap or protein particles in the total system; and the other values are measures merely of the physicochemical properties of a dilute solution formed because some of the water in the total system was left uncombined and soap or protein dissolved in it and was hydrolyzed.

No physical chemist has ever found any direct or simple relation between any one of the properties of the dilute solution phase of a lyophilic colloid system (its pH, its osmotic concentration or its electrical properties) and the "behavior" of the total system. And such a relation is not likely to be discovered for these physicochemical values measure merely the properties of one phase in a total system in which a more fundamental relation is that existing between this phase and a second phase—that of their mutual solubility.

In colloid chemistry a system like nitrocellulose/ether-alcohol or rubber/benzene or gum/water or starch/water is as "typical" of the lyophilic colloids as any other that may be devised and yet such systems have received little attention from the dilute solution chemists. This is because in all such colloid systems those properties so painfully analyzed for by the physical chemists disappear. Electrical properties, ions, isoelectric points, DONNAN equilibria and pHs and C_Hs, all pass out of the picture. But typical lyophilic colloid systems remain because mutual solubility remains.

Consideration of these facts will show why we have maintained that the greatest caution is required in making deductions from perfectly good physicochemical measurements as made upon such systems. The methods are being misused. A batch of dough, a soap vat, the soil, plastic masses, resins, varnishes and gums, the proteins, higher carbohydrates and the fats and lipoids simply cannot be "analyzed" by such methods.

As soon as we arrive at the level V of Fig. 2, the solvated colloid phase becomes the external phase and from here on to the lowest level, the total system is dominated by the physicochemical characteristics of this phase. This inverse type of solution does not show (1) a "normal" electrical behavior, (2) a "normal" reaction to indicators, (3) a "normal" refractive index, nor (4) a "normal" solvent property for any third substance.

We believe that the chemist who tries to "control," say an industrially important reaction mixture of the types here listed, will have to bear these things in mind. Of primary importance will be his determination of the level in our diagrams at which his mixture lies. This will indicate to him, in any mixed system, which is the external and which, the internal phase. And his conductance, potentiometric, indicator and osmotic measurements will then be measuring in essence either the properties of an ordinary true solution of x in a solvent or those of a solution of the solvent in x and it is the properties of the latter which give character to the lyophilic colloid system.

II. On the Greases

In a previous section[1] we used the lyophilic colloid systems that result when the chemically and electrically dead paraffins are mixed with various metal soaps as evidence for the notion that mutual solubility of the constituents is *the* factor which determines the possibility for the production of such systems and their stability. We wish now to turn the matter about and indicate how a knowledge of the values of such mutual solubility at different temperatures "explains" the production and the characteristics of the "greases."

[1] See page 164.

The first greases of commerce were simply those mixtures of high melting point fats which occur naturally (mutton tallow, suet or vegetable oil "stearins"). Chemically they were therefore mixtures merely of several glycerids. As such they were from the start mutually soluble systems in the sense of these pages, the mixtures fluctuating, with changes in temperature and relative concentration of the constituents, from "solutions" at higher temperatures of fat A in fat B which on cooling changed to "solutions" of inverse type with various "emulsions" or "suspensions" appearing as intermediate systems.

The earliest "synthetic" greases were mixtures of animal or vegetable fats with the mineral oils. Here again the mutual solubilities of the two kinds of "oil," their relative amounts, their liquid or solid character and the temperature determined whether the one was dissolved molecularly, was emulsified or was suspended in the other; or conversely.

In the greases of most recent date metal derivatives of the fats replaced the glycerids. Every kind of "soap" has therefore been mixed with every kind of mineral oil to yield the cosmetic creams, the shampoos, the insecticide mixtures, all kinds of cleansing "crêmes," various varnishes, the cutting oils and all those "greases" of commerce which vary from such as have the viscosity of water to waxlike cakes.

What has been written in the preceding pages gives us an understanding of what is accomplished when such greases are manufactured and what must be the nature of the resulting products. While grease manufacturers still carry their methods as secrets there is really nothing secret about them. In all instances, a metal soap is either (a) produced in their grease mixture or (b) added to a given oil. In the former instance a fatty acid or a mixture of such (for example "stearin" or "rosin") is first "dissolved" in the oil and then there is added a chemically necessary equivalent of some alkali (maybe caustic soda or, more commonly, lime). The net result is the production of a light metal or an alkaline earth metal soap which by the aid of heat is made to dissolve *in* the oil. Upon cooling, the mixture increases in viscosity or "sets" into a lyophilic colloid system owing to the reversal in the type of "solution" as discussed in these pages. The latest "inventions" in grease manufacture

start with a metal soap of known composition (like aluminium stearate) and with the aid of heat "dissolve" this compound in the chosen oil. On cooling, the soap falls out of solution, becomes solvated and the succession of colloid-chemical changes follow that have already been described.

It will be seen, therefore, that two variables, mainly, determine the ultimate result—the nature of the metallic soap employed and the properties of the oil. The soap itself varies with (a) the nature of the metallic radical and (b) its contained fatty acid.[2] Aluminium (because it stands highest in solvation capacity) is therefore found to be a better "stiffening" agent than calcium or barium; and stearates are more effective than oleates. In an otherwise chemically identical series the higher boiling point fractions of any oil yield a more solid ultimate compound than the lower members.

When water appears in a "grease" mixture (either as the product of chemical reaction or because added from without) the picture as described is complicated by a third variable, the result chiefly of the solubility of the water in the soap. The net effect is not only a competitive play of the soap for solvation by the water or the oil, but that which results from the solution, emulsification or suspension of this hydrated soap in the oil-solvated soap or the free oil. How this factor must influence, with changes in temperature, etc., the viscosity,[3] solvent, "wetting" and other properties of the ultimately formed "grease" is readily foreseen by any colloid chemist.

III. On The "Livering" of Paints[4]

The tendency of ready-to-use liquid paint mixtures to set into liverlike masses or, to express the total problem in more conservative terms, the tendency of once fluid mixtures of pigment and oil to increase in viscosity upon storage even to the point of yielding almost solid rubberlike moulds of their containers has long been the subject of investigation. The process is analogous

[2] See page 167.

[3] Martin H. Fischer and Marian O. Hooker: Koll. Zeitschr. *18*, 136 (1916); Fats and Fatty Degeneration, 40, 78 New York (1917).

[4] Martin H. Fischer and Werner J. Suer: Kolloid Zeitschr. *60*, 71 (1932)

to the formation of "grease" and the theoretical explanation that has been given of the behavior of such systems[5] is directly applicable to the problems of paint manufacture. We hold that with his knowledge of what chemical constituents (in both pigment and vehicle) entered into the composition of his finished product the manufacturer may know in advance when to expect livering.

Livering occurs whenever conditions in a paint mixture are such as to allow of the formation of a solvatable colloid. This compound becomes solvated by the paint vehicle and as this occurs the total mixture increases in viscosity, may become semi-plastic, and, in extreme cases, go hard.

The following three simple items govern the total problem.

1. Livering is due primarily to a change in the paint vehicle and is independent of the nature of the paint base except as the latter can or cannot react with the vehicle.
2. When increase in the viscosity of a paint mixture is not dependent upon a "spontaneous" increase in the viscosity of the vehicle itself (as when the viscosity of a raw linseed oil is increased through polymerization or oxidation) the livering process is dependent upon the formation of a metallic soap. The possibilities for the formation of this soap lie in (a) the reactivity of the materials constituting the paint base and (b) the availability of fatty acids present in or derivable from the vehicle.
3. The quantity and kind of metallic soap thus formed then determines the severity of the livering process, "severity" being a measure of the solvation capacity by the paint vehicle of the soaps formed. The soap does not dissolve in the vehicle and thus bring about an increase in viscosity but, per contra, the vehicle dissolves in or unites with the soap formed just as in the case of grease formation.

Proof of the correctness of these three conclusions may be deduced from the facts of practical paint manufacture and laboratory study. The following remarks are limited to the instance of the *oil paints*,[6] embracing under this caption all those

[5] See the preceding section.

[6] They may in principle however be applied to any of the moist water-colors in pans, tubes or cans. These also "thicken" or "set," though discussion of the process is usually dismissed by saying that they "dried out" in spite of the fact that the container was never opened. In these systems water takes the place of oil and a hydratable colloid the place of the generic solvatable colloid of the oil mixtures. The hydratable colloid

products in which the particles of a colored material are held together by any kind of an oil binder, from the thin soups commonly employed in interior house painting through the viscid enamels to the thick pastes that make up the fine arts tube colors and printing and lithographic inks. The vehicle or binder in all these instances is some kind of a drying (oxidizable) oil or varnish (in either instance a fat or a series of fats) diluted with more or less of some more volatile "solvent" like a lower boiling point fat (turpentine) or a hydrocarbon (naphtha, benzene, toluene). So far as the paint base is concerned chief interest centers in the question of whether it is a "lake" or not. In the case of the mineral pigments the nature of the chemical compound is paramount; in the case of the lakes it is not the color-giving constituent that is of much importance but the chemistry of the (usually) colorless base upon which the "lake" was "precipitated."

Certain paint mixtures never liver (if oxidation or "sulphuring" of the vehicle through exposure to air is avoided.)[7] This is because in the paint mixture no metallic soaps are formed and no other compounds are produced to become solvated by the vehicle. The cadmium sulphids, the mercury sulphids or the cadmium selenids when ground in linseed oil, any other drying oil or an oil polymerized by boiling but containing no drier (the "stand" oils or lithographic "varnishes") never liver. The statement holds also for barium sulphate, the purer lithopones and the chromates of zinc, barium or strontium. When the last

introduced into the moist water color (a carbohydrate or a protein or a soaplike compound produced during storage) and originally dissolved in the water becomes a solvent for the water and as this progresses there follows an increase in viscosity or the "livering" of the total mixture.

[7] "Blown" (oxidized) oils in general yield more viscid paint mixtures than the merely polymerized (boiled) oils and these more than the corresponding raw oils. The change from a (fresh) liquid paint film to a solid (as when any ordinary "drying" oil "dries" through oxidation) is not ordinarily spoken of as a livering process and yet in principle that is what it is. The sulphur present in various paint mixtures acts upon certain oils as does oxygen, yielding "vulcanized" oils which like vulcanized rubber are harder than the untreated material. It is such action of the sulphur in the ultramarines that makes these paint mixtures always "dry out," "go hard" or "liver."

named are not pure, some oxidation of the drying oil may occur and therefore some increase in viscosity but except for these rather trifling changes nothing happens with time to increase the viscosity of the vehicle and therefore nothing happens to the total paint mixture. The chemical composition of the paint base in all these illustrations is also such that no reaction can occur with the oil of the vehicle. No metallic soaps are therefore produced in the process of storage which can in any way change the composition of the original paint mixture.

Certain other paint mixtures always liver. In many instances this end is actually desired in order to obtain paint mixtures of better "body" than those first produced when pigment and oil are ground together, though an increase in viscosity even in these mixtures to the point of going solid is not desired. The paints most likely to liver are those carrying the hydroxids, the oxids and the carbonates of various metals. The hydroxids will (slowly) liberate fatty acid from the most neutral of oils; the oxids will do it almost as rapidly, especially if traces of water are present. For this reason zinc white, titanium white, or aluminium hydroxid all increase in viscosity or "liver," even when ground in the most neutral of oils. But the carbonates, which in themselves show small power of decomposing the neutral fats, will combine with free fatty acids and do this when such are present in non-neutral oils. For this reason the lead whites (essentially lead carbonate) have long been known to increase in viscosity on storage; but the same is true when chalk is used as the pigment of a white paint or as an "extender" of any other white or colored paint base. Barium sulphate, magnesium silicate and various clays (which in paint mixture do not lose their "neutrality") when used as such extenders do not favor livering because even when free fatty acids are present in the oil these compounds do not react with them. In all these instances livering occurs or does not occur depending upon whether free fatty acids are produced or are present with which the base of a metallic hydroxid or carbonate may combine to yield the corresponding metal soap.

These facts indicate that livering occurs only in such paint mixtures in which the possibilities are existent for the production of metal soaps.

Half this factor is obviously present from the start if the vehicle into which a given paint base is to be ground contains free fatty acid. Any unrectified raw oil is likely to carry several per cent of such free acid which explains why such oils have always had the reputation of a greater likelihood to liver than oils treated with alkalies to remove such acids; and why heat treated oils (even when no driers were added) have a livering value beyond that of the untreated. It is for this reason that the high acid number (the titration value for the free acids) has so frequently been declared an index to the livering possibilities of an oil (even though the statement has almost as frequently been denied). Thus P. E. MARLING,[8] speaking for a series of coworkers, found in tests upon the livering propensities of ten oils with zinc oxid that livering was quite uniformly greater (a) in such oils as carried the highest free acid values and (b) in such as were from the start most heavily "bodied" either through polymerization or oxidation. With hardly an exception he found the acid value of a given oil to be lowered, and progressively with time, when zinc oxid was ground into it. And yet the first of his general conclusions was that "the acid number of an oil had no bearing on its probable behavior with zinc." More recently the hydrogen ion concentration[9] has been studied as the index of livering value. Everyday paint manufacturing experience indicates that neither of these values is a guide. Such is the case, obviously, because neither figure tells us anything of the *kind* of fatty acid present and, of course, nothing regarding the *base* to be ground into the oil and hence the kind of soap likely to be formed. A cadmium sulphid or a barium sulphate will not liver no matter what the titration or hydrogen ion acidity of an oil; and any lake on an aluminium hydroxid base, even when ground into the most neutral of oils, will. In the first instance the fatty acids though present have no base to unite with; and in the second, the base in time cracks its own fatty acids out of the oil even though none was present originally.

[8] P. E. MARLING: Am. Paint and Varnish Assoc. Circular No. 319, 535 (1927).

[9] See, for example, B. P. CALDWELL and J. MATTIELLO: Ind. and Eng. Chem. Anal. Ed., *4*, 52 (1932).

That half of the problem of metal soap production upon storage which has to do with the kind of base present has already been touched upon. Pigment mixtures carrying hydroxids are most likely to liver, with the oxid and carbonates following (aluminium hydroxid against lead oxid against lead carbonate, for example). Union with the fatty acids, either present from the start or produced during storage, is easy in all these instances. But if the pigment is a sulphate or a chromate or a sulphid, possibility of such union with the base of the pigment is enormously reduced (as witness the absence of all reputation to liver in the case of lead chromate against lead oxid, of barium sulphate against barium carbonate or zinc sulphid against zinc oxid).

Having stated in this fashion the conditions most favorable to the production of metal soaps we have now to say why their appearance in a paint mixture is followed by livering. It has been said that solution of the metal soaps in the paint vehicle is responsible; actually, livering depends upon an exactly opposite type of reaction—the vehicle dissolves in the soap (or, put another way, solvates the soap or combines with it). The new "solution" is more viscid than the original vehicle or actually solid, wherefore the total paint mixture is more viscid or actually "livered."

The livering propensities of any metal soap depend upon (a) the nature of the fatty acid in the compound and (b) the nature of the base. Any saturated fatty acid (like stearic) induces greater livering than the corresponding unsaturated acid (oleic); and when soaps carrying the same fatty acid but different bases are compared, aluminium ranks first. Experimentally the cadmium soaps take second place though in practice they are of little importance since the cadmium compounds used in paint manufacture do not lead to cadmium soap formation. Magnesium ranks third and is of great moment when non-neutral magnesium compounds constitute the paint base (magnesium xanthinate, true Indian yellow) or are used as fillers, extenders or in the base of lakes. The soaps of calcium, barium and strontium all liver oil, though in practice calcium is probably the most important item because so often employed as a paint base in the form of the carbonate. Barium carbonate takes a similar posi-

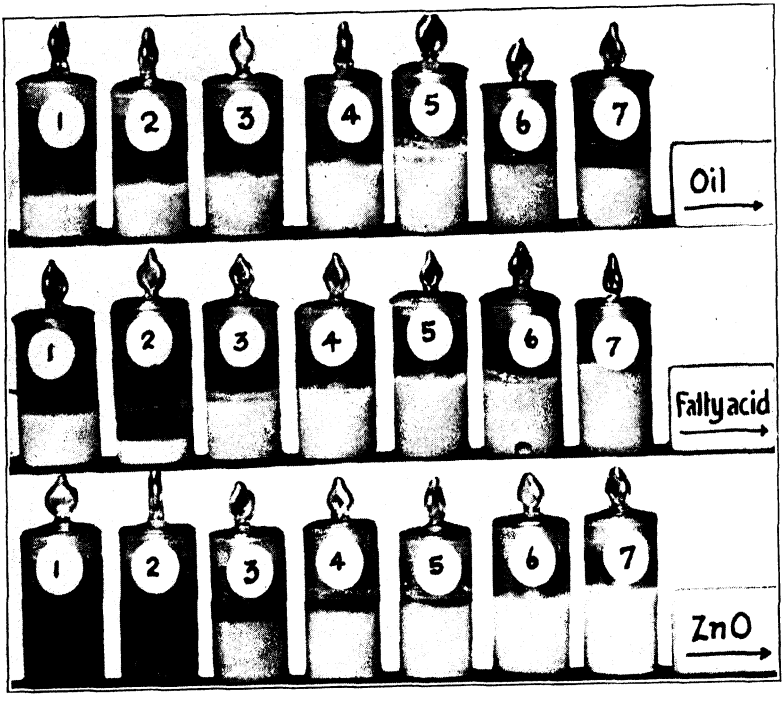

FIG. 77

tion. Strontium and barium as the chromates, are without significance and so is barium sulphate because inactive if neutral.

These facts make it clear that the various metal soaps liver the true fats (from the thin fluid oils to the almost solid "varnishes") as, in similar fashion they "liver" the hydrocarbon oils in the manufacture of "greases." The parallelism between grease formation and ability to liver an oil is in fact so great that we suggest that for laboratory testing the ordinary hydrocarbons (benzene, toluene, xylene) be used in place of the fatty oils (which, chemically, are less likely to be of uniform composition and more likely to suffer changes of oxidation, polymerization, etc., during laboratory handling which cloud the final results).

We wish now to give some examples out of laboratory experience which verify in quantitative fashion the truths expressed as generalities above.

1. Livering parallels the possibilities resident in any paint mixture for the production of a solvatable metal soap. This is illustrated in Fig. 77. There are shown in the first of the three series of paint mixtures the effects of grinding unit mixtures of zinc oxid (0.84 g.) and linseed oil fatty acids (6 g.) into increasing volumes (0 to 12 g.) of acid-free linseed oil. The possibilities for the formation of zinc soap are the same in all but livering occurs only in tubes 1 to 4 since in these only are the solvation capacities of the soaps equal to taking up all the proffered vehicle. In the second series, the quantities of zinc oxid (0.84 g.) and oil (10 g.) are fixed but the amounts of linseed oil fatty acids increase from zero in the left-hand tube to 6 g. in the right-hand one. The increase in fatty acid makes possible progressive increase in the amount of zinc soap formed which, absorbing the vehicle, yields a series of increasingly viscid paint mixtures which go solid in 5, 6 and 7. In the third series, increasing amounts of zinc oxid (0 to 0.84 g.) are ground into standard volumes of a definite mixture of oil and fatty acid (10 g. acid-free linseed oil + 6 g. linseed oil fatty acids). The mixtures liver in tubes 6 and 7, in other words as soon as sufficient zinc soap is producible to take up the vehicle.

2. An already livered paint is brought back to fluid form only with great difficulty because in the more serious cases it requires enormous additions of the vehicle to satisfy the solvation capacity of the metal soaps that have been formed. A livered paint is one in which, after primary formation of a metal soap, this has turned about and become a solvent for the vehicle. In the ordinary mixed paint the relation of the various constituents to each

other is such that the possibilities for the formation of metal soap are large while the amount of vehicle available for its solvation is small. In other words, the livering *capacity* of the total mixture is far from satisfied. The quantity of this factor may be determined by permitting a mass of livered paint access to more vehicle. The amount that it will "swell" is then the measure of this factor. Its value is indicated in Fig. 78. The mass of a (livered) madder lake (alizarin precipitated upon aluminium hydroxid) shown in the lower half of the figure has, in three days, absorbed more than four times its initial weight of vehicle and is still solid as shown in the upper half of the figure. For such a test linseed oil may be used though the less viscid turpentine or a hydrocarbon like benzene allows the end values to be reached more quickly.

3. The effect of the kind of metal soap formed upon the extent of the livering is indicated in Figs. 79 and 80. The lower half of Fig. 79 shows the appearance of definite volumes of acid-free linseed oil (50 g.) immediately after the addition of molar equivalents (1/100 gm. mol.) of three different zinc soaps. The mixtures were warmed for an hour. Their appearance three days later is shown in the upper half of the figure. The originally thin sediments of the laurate (L) and stearate (S) have "swollen" to the heights seen in the photograph. The oleate (O) has also absorbed oil to the extent of becoming transparent though the volume increase for the unsaturated acid is always less than that shown by the corresponding saturated fatty acid. The livering values of the metal soaps rise to enormous proportions when a base like aluminium takes the place of zinc. The effect is shown in Fig. 80. The lower series of tubes evidences the liquid nature of the mixtures that result immediately after mixing 1/100 gram molecular weights of the laurate, myristate, stearate and oleate of aluminium with 50 grams of acid-free linseed oil. After warming, and several days later, livering is so extensive in these 4 to 6% mixtures of the soaps with the oil that except in the oleate, the entire volume of oil has gone solid as evidenced in the bottles of the upper row of Fig. 80.

4. With given concentration and kind of metal soap the degree of livering varies with the type of vehicle used. In any chemically comparable series of oils there is an increasing tendency to excessive viscosity and to actual solidification of the mixture with every increase in the viscosity of the original oil. A turpentine paint therefore increases in viscosity less than a raw linseed oil paint, and this less than a boiled linseed oil (an oil thickened through mere heating but without change in its acid number and free of driers). Such an oil is said to be polymerized. From a theoretical point of view it may therefore be con-

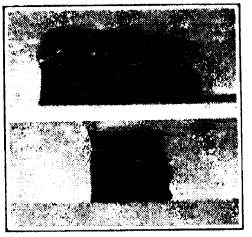

FIG. 78

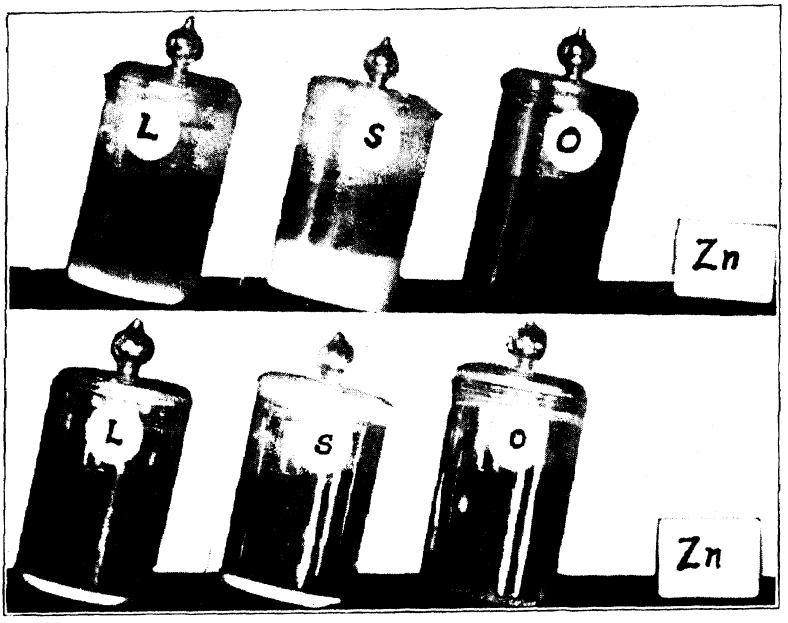

FIG. 79

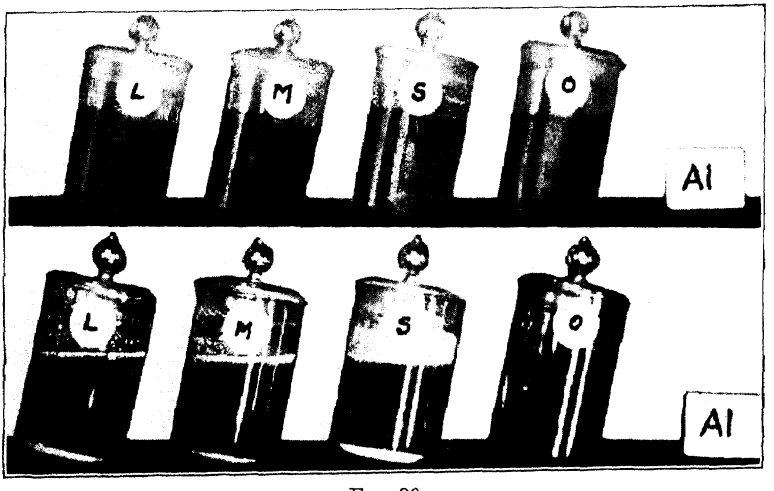

FIG. 80

cluded that the fat molecules are larger and that solvation of a given metal soap by such larger molecules "explains" the greater viscosity of the resulting paint. But in the ordinary boiling of an oil the thickening is accompanied by a progressive increase in the acid number. When such an oil is compared with another made by taking the original oil but raising its acid number to that of the boiled oil through addition of the fatty acids derivable from that oil, even though both oils show the same initial viscosity, the boiled oil yields a more viscid paint than the unboiled. The matter can only be accounted for by saying that the available acids in the two oils are different. This chemical difference explains, at the same time, why the hydrogen ion concentration or the acid number of any oil can never by itself become a correct indicator of the livering propensities of that oil. Boiling will increase not only the viscosity of a neutral oil but that of the fatty acids derivable from that oil. If the explanation given for the one is applicable to the other then it must be said that heating not only polymerizes fats but fatty acids as well. And in explanation of the higher viscosity derivable from a heat treated and more acid oil over a similarly acid but untreated oil we may call upon at least two factors, that of the larger moleculed oil and that of the larger moleculed soap derivable from the first as compared with the second.

PART THREE

BIOLOGICAL APPLICATIONS

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I. Introduction

In the first half of this volume the nature of the lyophilic colloid was discussed as an end in itself. We propose now to show the usefulness of the findings and concepts there developed for a better understanding of what goes on in living matter.

Since the monumental studies of Schwann and Schleiden, the histological analysis of living matter—both vegetable and animal—has yielded the general truth that all living matter is composed of cells. Since that day, physiologists, whether of the school of the general or the special, are agreed that an understanding of what goes on in living matter must be synonymous with an understanding of what goes on in the single cell. And it is for this reason that there has constantly recurred to all biological workers this fundamental question: *what is the nature of the physical or chemical system that constitutes living matter?*

The oldest physiologists answered by saying that it was composed of "protoplasm" to which were attached, or in which were inherent, certain "life principles," the latter incapable of any analysis in the terms of physics and chemistry, and the former but little more so.

We owe a first step forward in the scientific analysis of the problem to the chemists, who by the end of the last century had shown that all living cells (all living matter, in other words), were reducible to five great classes of compounds—the proteins, the carbohydrates, the fats, the salts, and water. But the attempts to resynthesize from such materials any kind of system which would manifest the physical or chemical properties exhibited by the living mass proved disappointing.

It was at this stage that the physical chemists brought the fruits of their study to bear upon physiology. They had established the laws of the dilute solution—the laws of diffusion, of osmotic pressure, of electrolytic dissociation, of reaction velocity, of equilibrium—and it was a common occurrence to find one of their number chiding the physiologist of thirty years ago for

his ignorance of these laws; for, as the physical chemists maintained, protoplasm was nothing but a dilute solution, and to know the laws of the dilute solution was, by corollary, to know the laws of protoplasmic behavior.

This point of view continues into the present. The following is quoted from almost the opening sentence of such a physico-chemically inclined physiologist: "Protoplasm contains sixty percent of water"—he might have said eighty or even ninety-nine, and so strengthened his argument—"therefore it is a dilute solution, and all the changes which take place in it must be governed by the laws of the dilute solution."

What sort of system do these accepted apostles of modern physiology tell us that the cell is? In plain words they maintain that it is a drop of water. In this they assume to be "dissolved" the various salts found in protoplasm as well as various non-electrolytes, like sugar and urea. They degrade the proteins to a third place (the pure chemists always mentioned them first because they knew them to be *the* universally present and *the* characteristic elements of all living matter) simply because they are passive under the ordinary laws of the physical chemists. The fats and carbohydrates—especially the higher ones—are added as afterthoughts, as additional materials which, with the proteins, are "suspended" in the water.

The mixture of the physical chemist turns out little better, however, than the similar mixture of the pure chemist. To get a "behavior" out of it at all comparable with that of a living cell, a further element is therefore called for, and this the physical chemist does not define in chemical terms, but only in physical. It is the "membrane" that he assumes to surround his droplet and which, depending upon the author, is "semipermeable," "plasmatic," or "fatlike." This membrane bears no relation, of course, to the anatomical cell wall which surrounds certain cells, more particularly the vegetable cells, for such cell walls are not the carriers of any "semipermeable" properties. In the case of such vegetable cells, for example, the physiologically active "membranes" of the physical chemists are therefore placed in the "primordial sheath" or surface layer of the protoplasm of the cell lying *within* the anatomical cell wall.

The colloid chemist thinks most of these things wrong. In order to get the issues straight, suppose we ask him to state in like categorical fashion what he holds a cell to be. He begins by wiping out the cell "membrane" of the physical chemist because entirely hypothetical. With the pure chemists, he places the proteins of the living mass first. He mentions next the salts, but not as things which are merely mixed into the protein but as materials which, as acids or bases, were originally *united with* the protein. Third, he puts the water, but not as a solvent *for* the protein-salt complex but as a material dissolved *in* the latter. *This membraneless hydrated protein-salt compound is the unit of his living mass.* Into it (for the present) he merely mixes (emulsifies) the fats and the higher carbohydrates which are found in cells.

This recitation of the points at issue is not a mere play with words. In what is here stated as the colloid chemists' side of the question is buried the right or wrong of long chapters in physiology and pharmacology, of pathology and medicine, and not a little of the hope or the heartburning which goes with the application of laboratory methods to clinical diagnosis.

II. Criticism of the Osmotic Concept of the Cell

It is no accident that the proteins are the universally present constituent of all living matter and that its one indispensable food (both for growth and maintenance) is protein or something out of which this may be made. Nor is it an accident that there is no life without water and no life without inorganic substance of which either too little or too much kills.

What is the relationship between these three indispensable units of the living mass? They can obviously not be merely mixed together as the analytic biological chemists once thought, for such simple mixing leads to nothing which either physically or chemically is reminiscent of living matter. There is a closer tie of the one to the other.

The physical chemists urged a first opinion in the matter when they said that living cells were systems or arrangements osmotic in type, and established their concept by pointing out the large number of analogies existent between living cells and the "os-

motic" cells of the laboratory. Both types of cells absorbed water and lost water, for example, and showed a failure to be permeable to various substances dissolved within or about them—discoveries which superficially viewed, seemed to make for the identity of the two systems.

Suppose we go back to the years preceding 1907, and sketch the view of water absorption by protoplasm to which all subscribed then, and to which the majority still subscribes.[1] Aside from some "physiological" theories—which explain nothing—and the "pressure" and "permeability" theories of the pathologists (which can also explain nothing in that vast mass of living vegetable and animal matter that is without any circulatory system), all the biological workers of that time were dominated by the osmotic notion of water absorption. This osmotic notion, as first advanced by PFEFFER and DE VRIES for vegetable cells and developed shortly thereafter by OTTO NASSE for animal cells, was a clean-cut physicochemical concept. Since later workers have added nothing which is not merely a modification of this concept or, worse, a something which has confused the whole picture, it is well to get clearly in mind just what these first laborers in the field thought.

Concretely expressed, they held every cell to be a circumscribed mass of protoplasm surrounded by a semipermeable wall. The semipermeable wall was assumed to be comparable to those originally discovered and described by MORITZ TRAUBE and was *by definition* impermeable to all dissolved substances, but permeable to the solvent, water. They conceived of protoplasm as essentially water, in which there were "dissolved" various salts and non-electrolytes like sugar and urea. To materials like protein and lipoid, or starch and glycogen, they gave little attention, since they were incapable of exerting "osmotic pressure." According to the beliefs of PFEFFER and DE VRIES, cells took up water whenever immersed in distilled water or any solution possessed of a "tonicity" lower than the cell contents; or gave off water whenever immersed in solutions of higher "tonicity," according to the laws of "osmotic pressure." These laws are the laws of VAN'T

[1] See, for example, BALDWIN LUCKÉ and MORTON MCCUTCHEON: Physiological Reviews, *12*, 68 (1932).

HOFF that were enunciated *after* the experimental and theoretical "osmotic" studies of PFEFFER and DE VRIES and on the basis of their numerical data. They were modified later by ARRHENIUS' concept of the electrolytic dissociation of acids, alkalies and salts.

It is well to consider why PFEFFER and DE VRIES' clearly thought out concept of water absorption as applied to protoplasm met with difficulties, for to overcome such may well be said to have been the sole object of all the workers who since have tried to save the osmotic idea for physiology and pathology.

Difficulties arise from two sides, (1) from the purely biological and (2) from the purely physicochemical.

From the biological side it is sufficient to point out that an osmotically constructed living cell is an impossibility. If surrounded by a semipermeable wall, no dissolved substance could enter or leave it, which is to say that a cell could never take up its needed food (be it oxygen, salt, sugar or amino acid) nor rid itself of the products of its metabolism (like carbonic acid, urea or phosphate).

To meet such objection, it became popular to say that the word "semipermeable" was not to be taken too strictly. According to such compromisers, the "membrane" was made permeable to many things "necessary" for the life of the cell; or it was permeable at one time and not at another, as the author wished; or he made it permeable in one direction but not in the opposite, etc. The thing yielded a picture as complicated as the number of men who busied themselves with the problem. In biological reasoning, this fact, however, remained: in proportion as the semipermeable membrane was made permeable to dissolved substances, concentration differences between cell content and surroundings were equalized; and as this happened, nothing remained to move water. *A living cell is, however, capable of taking up and giving off water, and of taking up and giving off dissolved substances, and these two things may occur at different times or at one and the same time, and with the solvent and the dissolved substances moving in the same direction or in opposite directions.* Whatever may be held for or against any theory of absorption and secretion by protoplasm, this remains certain: until it can explain *all* these biological traits, it is not adequate.

From a physicochemical standpoint, the osmotic notion of water absorption by protoplasm fared even worse, for here the so highly prized "quantitative" experiments came into play—and failed. Were living cells true osmotic systems they should be equally affected, for example, so far as their volume is concerned, by isosmotic solutions of different salts. This they never are. If a sodium chlorid solution of a certain strength just preserves the normal volume of a plant or animal cell, an osmotically equivalent solution of potassium chlorid usually permits it to increase, while the chlorids of magnesium, calcium and iron lead to shrinkage. Again, by the laws of osmotic pressure, unit increments in the concentration of any salt solution should lead to unit decreases in the volume of a cell; as a matter of fact, the amount of shrinkage is progressively less with every such unit increase. Finally, certain substances, like the acids and alkalies, act upon living cells in contravention to all laws of osmotic pressure. They make cells take up water until they have swelled not only beyond the bounds of their normally calculated osmotic pressure but beyond such as has been calculated for them (OVERTON) on the assumption that all their proteins, carbohydrates and fats are split into smaller (and therefore osmotically active) molecules through acid or alkali.

The original masters in physiology who devoted their lives to the establishment of the osmotic concept of water absorption by living cells were familiar with many of these facts and therefore never held to the adequacy of their concept with half the passion of more modern workers upon their idea. PFEFFER, for example, knew that the osmotic notion did not explain all his biological observations and suggested that "imbibition" might play a rôle; and OTTO NASSE, intent on discovering whether muscle behaved as an osmotic system, decided it did not, when he observed how intensely acids made this material swell. FRANZ HOFMEISTER, in the early nineties, held the "water-attracting" action of salts upon gelatin plates to be comparable with the cathartic action of these salts in pharmacology, but his ideas were spurned by a generation which saw physiological progress only in the application to protoplasm of the physical chemists' dilute solution laws (which, in major portion, promptly proved themselves not to fit).

III. The Colloid-Chemical Theory of Water Absorption

It was with the problem in this state that, in 1905, we turned to an experimental study of factors other than the osmotic which might aid in the solution of the total problem. We thought that the hydrophilic colloids, more particularly the proteins, played a rôle, and suggested that in their swelling and their shrinkage lay a large fraction of the explanation of the problem of why living cells hold any water at all; and why, under physiological and pathological circumstances (edema) this quantity may vary. Two years of work yielded little to convert our hypothesis of colloid water absorption into an experimentally founded theory until one afternoon, while busy upon a related problem, we discovered a fact[2] which at once explained all the experimental findings which until then had stood against the establishment of a colloid-chemical theory of absorption and secretion.

As the importance of the fact and its necessary corollaries are not yet clear to many of our critics, we inject this personal history. We were trying to prove that peptic digestion under the influence of different acids was not, as then generally believed, dependent upon the action of the different acids upon the ferment but *upon the protein* and we were looking for a parallelism between the order in which the acids affected proteolysis and the order in which they induced some visible change in the protein. With fibrin used as the protein to be digested, a parallelism between the rate of digestion and the degree of its swelling was quickly established. In trying next to say why sulphuric acid was the poorest digester (and produced the least swelling), while hydrochloric was the best (even when employed in the same ionic concentration), we naturally concluded that the SO_4 radical had to be responsible. If this conclusion was correct, it was therefore to be expected that the addition of a neutral salt containing SO_4 to a hydrochloric acid should not only reduce the proteolysis but also the swelling. When experiment verified this conclusion, we had discovered *an antagonism between acids and neutral*

[2] Martin H. Fischer and Gertrude Moore: Am. Jour. Physiol., *20*, 330 (1907).

salts in a physicochemical system of known composition which immediately made clear many a similar physiological antagonism.

This experiment pointed the way for the overcoming of the last difficulties in the establishment of the colloid-chemical notion of water absorption for, in the swelling action of acids upon proteins and in the effects of neutral salts in the reduction of this swelling, there appeared at once not only all the possibilities for explaining that behavior of living cells (their excessive swelling under the influence of acids) which had previously not fitted in with the laws of osmotic pressure, but all those phenomena as well (the specific effects of different salts at various concentrations) which had formerly been accepted as proof for the tenability of the osmotic concept.

The statement is made because such findings were not originally anticipated. We had expected only to unearth something which would modify or add itself to the osmotic concept of water absorption. The experimental observations on colloids relegated the osmotic notion to a secondary place and, in our opinion, it has today lost all significance for the problem of water absorption and secretion (as well as for the absorption and secretion of dissolved substances) by normal living protoplasm.[3]

Upon what, now, does the colloid-chemical theory of water absorption by protoplasm rest? It rests *upon the qualitative and quantitative analogy between the laws which govern the taking up and giving off of water by any simple protein colloid* (like fibrin, gelatin, aleuronat, wheat protein, etc.) *and the laws which govern the absorption and secretion of water by any cell, tissue, organ or organism.* These laws as established for fibrin, for example, may be summarized as follows:[4]

1. Fibrin absorbs more water in any solution of acid or alkali than in pure water, the amount of such absorption increasing progressively, up to a certain point, with every increase in the concentration of the acid or alkali (see Fig. 81A).

[3] The one place where in *pathology* it may, in totally modified form, play a rôle, has been discussed elsewhere. MARTIN H. FISCHER: Soaps and Proteins, 246, New York (1921).

[4] MARTIN H. FISCHER and GERTRUDE MOORE: Am. Jour. Physiol., *20*, 330 (1907); MARTIN H. FISCHER: Pflüger's Archiv., *124*, 69 (1908); *ibid.*, *125*, 99 (1908).

2. The addition of any salt, even a neutral salt, to such acid or alkaline solution reduces the amount of swelling, and this (a) according to the concentration of the salt added and (b) its kind. Increase in concentration progressively diminishes swelling (see Fig. 81B); while at the same concentration, comparative experiments show that the acid radicals follow the order, chlorid,

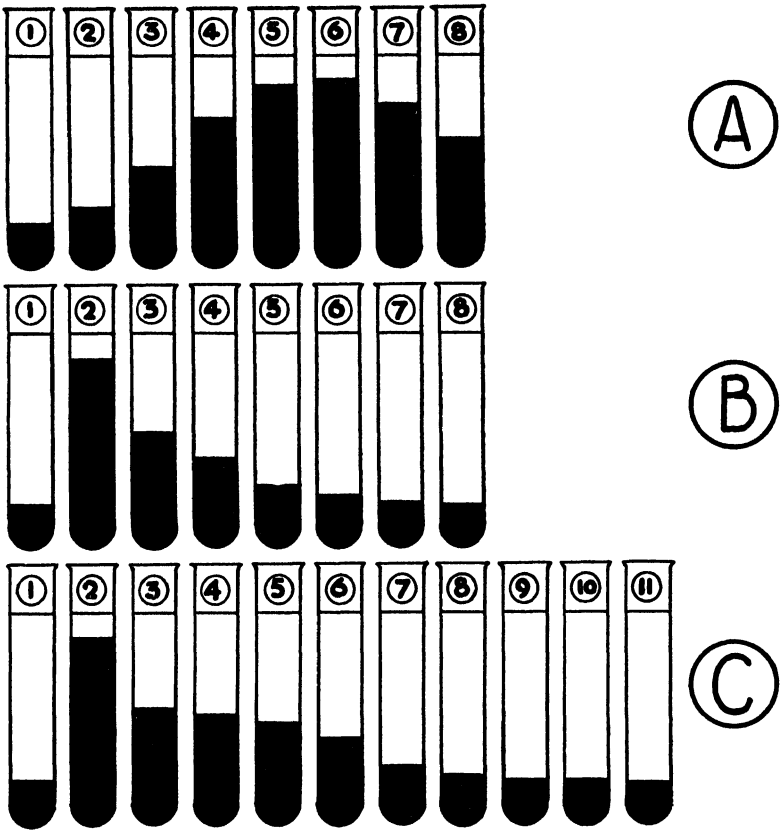


FIG. 81

bromid, iodid, acetate, sulphate, phosphate, citrate (see Fig. 81C), while the alkali radicals succeed each other as NH_4, K, Na, Li, Mg, Ca, Sr, Fe, Cu, Hg, when the least powerful dehydrator is mentioned first in each instance.

3. The non-electrolytes (sugars, urea and the alcohols) even at the same "osmotic" pressure are much less active in reducing the swelling of fibrin in the presence of an acid or an alkali than are the electrolytes.

4. This taking up and giving off of water is in large measure reversible.

5. Of substances other than the acids or alkalies which increase the water absorbing power of fibrin may be mentioned urea, pyridin and various amins. The increased hydration capacity induced by these substances is, however, different from that produced by acids or alkalies, for it is *not* markedly reduced through the addition of neutral salts, but it is reduced through the presence of the sugars which affect acid or alkali swelling relatively little.

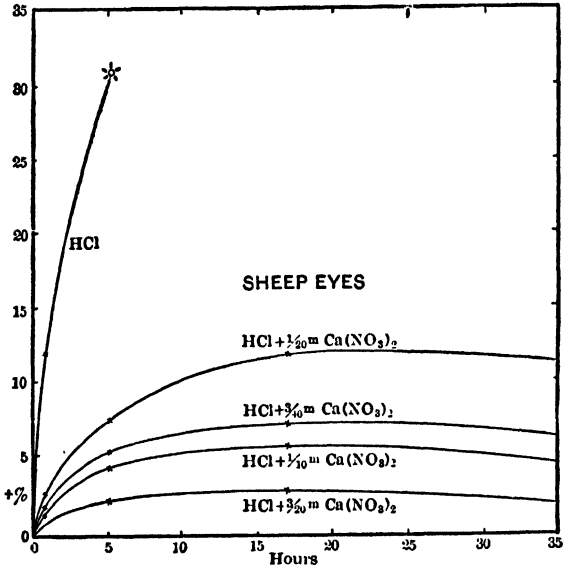


FIG. 82

An entirely similar set of laws may now be established not only for every other protein (gelatin, gluten, aleuronat, casein) but, what concerns us more, for every cell, tissue, organ or organism.[5]

The isolated cells of the blood, tissues like muscle, brain or spinal cord, and whole organs like the eye behave exactly like granules of fibrin or masses of gelatin. Two sets of swelling curves, as established for the eye, may serve to illustrate the parallelism better than many words. In Figs. 82 and 83, time

[5] MARTIN H. FISCHER: Pflüger's Archiv., *124*, 69 (1908); *ibid.*, *125*, 396 (1908); *ibid.*, *127*, 1 (1909); MARTIN H. FISCHER and MARIAN O. HOOKER: Kolloid-Zeitschr., *10*, 283 (1912). A running account may be found in Œdema and Nephritis, 3rd Ed., New York (1921).

is plotted on the horizontal, and degree of swelling in percentage increase in weight over the original, on the vertical. In a pure acid, the eye absorbs enough water to burst—an experiment which showed for the first time how "glaucoma" could be produced at will and of an intensity never observed clinically. The addition of any neutral salt reduces this swelling, the amount of this reduction increasing with every increase in the concentra-

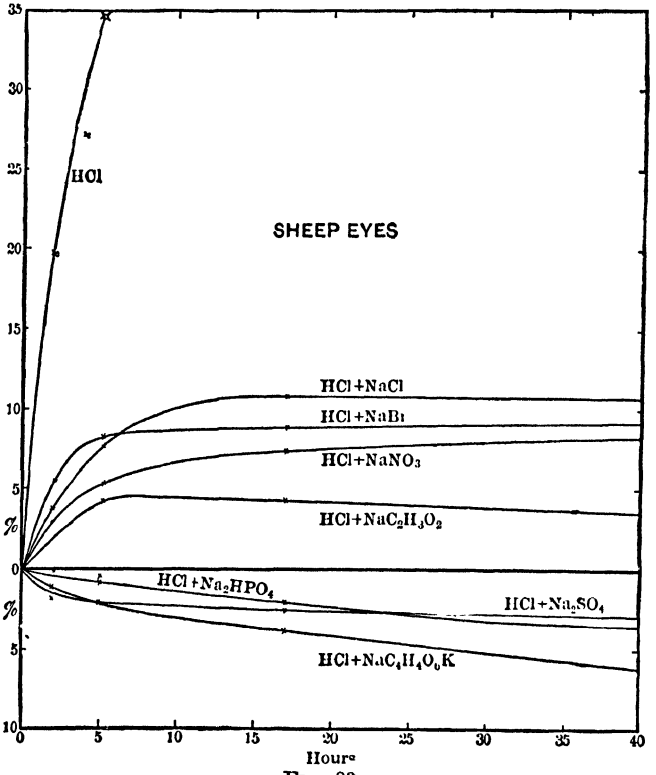


FIG. 83

tion of the added salt (Fig. 82) while the order in which the salts are effective is that observed when pure proteins are studied (Fig. 83). In this antagonism between acids and neutral salts is given the foundation for a proper therapy of this disastrous disease. As the diagram shows, a proper salt, when used in the right concentration, will not only keep an experimentally produced glaucoma from developing, but will actually make the eye

lose water. Instead of an increased "intraocular tension," the tension may actually be decreased to below the normal.

IV. Edema as a Problem in Colloid Chemistry

It is sometimes said that while colloid swelling and water absorption and secretion in living tissues thus parallel each other qualitatively, colloid water absorption is nevertheless inadequate to explain the higher grades of water holding power shown by tissues in edema. But the problem of edema is also a problem in colloid chemistry—that of the ways and means by which the normal hydration capacity of the body colloids is heightened.

The pathologists still uphold the teaching that edema is produced by changes in the pressure of the circulating fluids of the body (increased blood and lymph pressure) together with an increase in the permeability of the vessel walls. This pressure theory breaks of its own weight. Not only may we see extreme degrees of edema in organisms (plants) possessed of no circulation but mere increase in blood pressure (in animals, for example) never leads to edema. Again, extreme degrees of edema are encountered pathologically without any change in blood or lymph pressures; and measures which increase blood pressure and should therefore increase edema (caffein, quinin or digitalis in heart failure) are known to produce just the opposite effect. As a matter of fact the severest grades of edema that can be produced experimentally are created by doing away with all circulation. Remarks concerning "permeability" are mere plays with words in the hands of physiologists or pathologists for no such workers have ever paralleled their permeability concepts with any of the concepts of permeability known to a physicist, or a physical or colloid chemist.

In place of the pressure idea, we have to look to changes in the tissues and cells themselves for the first "causes" of an edema. The first experimentally supported suggestions in this direction were made by Lazarus-Barlow.[6] He and subsequent workers attempted to define the real nature of such changes by saying that they were osmotic in type and that increases in the osmotic pressure of the cell contents led to an increased absorption of water by the affected cells and thus to their edema. This

[6] W. S. Lazarus-Barlow, Brit. Med. Jour. *1*, 634 and 691 (1895).

osmotic theory of edema must be objected to on the same grounds as the osmotic theory of water absorption by cells under physiological conditions. Cells have no semipermeable membranes about them; and the amount of water held by edematous tissues is so large that there is not enough osmotic pressure available in the cells to account for all the absorption observed. But the severest grades of edema can easily be understood on a colloid basis.[7] A high grade of clinical edema is represented by a thirty percent increase in body weight; an eight percent swelling of the brain kills a man in coma, and a five percent increase makes him stuporous. While even these trivial edemas cannot be explained through increase in osmotic pressure, colloid swelling readily accounts for even the most extreme forms. We have made muscle or brain substance take up two hundred and fifty per cent its original weight in water. Taking one-quarter of normal tissue as its dry weight, we have it holding but three times this weight physiologically, or fourteen times this weight in the extreme experimental instance cited. How easy to explain these figures when it is remembered that simple protein colloids like gelatin or fibrin take up twenty to thirty times their weight of water under comparable circumstances, while other colloids (like the various soaps which have so much in common with the protein derivatives) hold even ninety-nine times their weight in water and still remain solid!

A state of edema is induced whenever, in the presence of an adequate supply of water, the capacity of the tissue colloids for holding it is increased above that which we are pleased to call normal. Any agency capable, under the conditions existing in the body, of thus increasing the hydration capacity of the tissue colloids constitutes a cause of edema. The accumulation of acids within the tissues, brought about either through their abnormal production or through the inadequate removal of such as some consider normally present in the tissues, is chiefly responsible for this increase in the hydration capacity of the colloids, though the possibility of explaining at least some of it

[7] MARTIN H. FISCHER: Physiology of Alimentation, 268, New York (1907); Am. Jour. Physiol. *20*, 330 (1907); Jour. Am. Med. Assoc., *51*, 830 (1908); Œdema, 186, New York (1910); Kolloidchemische Beihefte, *2*, 304 (1911).

through the production or accumulation of substances (of the type of urea, pyridin, certain amins, etc.) which hydrate colloids as do acids, or through the conversion of colloids having but little capacity for water into such as have a greater capacity must also be borne in mind.

V. On the Nature of the Relation Between the Proteins, the Electrolytes and the Water of the Cell

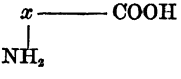
Having established in this way that any particle of protein (like a (membraneless) flake of fibrin or gelatin) takes up and gives off water in the same fashion and under the same conditions as any isolated animal or plant cell, and having classified this water absorption or secretion as of the same type as the hydration or dehydration of any hydrophilic colloid (the solvation or desolvation of any lyophilic colloid), we may now utilize the findings detailed in the first half of this volume (as those on casein) for a better understanding of what happens in the living mass. What has happened when a protein colloid has "absorbed" a certain amount of water or, when under the "influence" of an acid or an alkali, it has taken up a much greater amount; or when a cell, under identical circumstances, has behaved similarly? Many answers have been given to this question.

A lyophilic colloid entering into union with its "solvent" is usually said to have "adsorbed" this. The term, it should be remembered, does not "explain" what has happened but merely restates in a single word the mathematical relation existing between the two materials entering into union. If union between *a* and *b* is not linear but is better expressed by a curve, the process is declared to be an example of adsorption. Adsorption is universally accepted as a "surface" reaction but the explanation of what happens at or in the surface to account for the curve varies between two schools of extremists. The one believes in a purely "physical" union at the surface between the two materials; the other holds the union "chemical," maintaining merely that the "concentration" of the adsorbing reagent is to be counted as proportional not to its molar weight but to the amount of its (exposed) surface. In the latter instance the rela-

tion between the adsorbent and the adsorbed material would obviously remain "quantitative" and "stoichiometrical." We ourselves incline to the second belief, for when a neutral protein, for example, has taken up all the water it will, that water has been "dissolved" to a fixed value in the protein. The product may be either a "solid solution" as in the instance of fibrin, or a "liquid solution" as in the instance of various plant proteins. But in either case since the amount of dissolved water is fixed in its value, the union is obviously "quantitative" in character and such "solution" becomes by definition "chemical."

What change occurs in the total picture when upon the addition of an acid to a previously "neutral" protein, this is "influenced" to take up more water? The effect is usually ascribed to the action of the hydrogen ions. The absurdity of this constantly recurring generalization is all too evident. *No protein has ever been found in which swelling parallels the hydrogen-ion concentration* (with or without the assumption of a DONNAN equilibrium). *Acids when brought in contact with proteins unite with them* (as first emphasized by BUGARSZKY and LIEBERMANN thirty years ago) *to form a new set of protein derivatives each of which has a specific solubility for water and thus a specific capacity for "swelling."*

A (*partial*) explanation of what has happened between the protein, the electrolyte and the water may be discovered by recalling the chemical constitution of the proteins. They are (to the best of our present-day chemical knowledge) linkages of various amino acids. Many of these amino acids are amino-fatty acids, the empiric formula for any of which may be written as follows:



The x may stand for any chemical nucleus we choose. The addition of an acid or an alkali to such an amino-fatty acid will, by virtue of the NH_2 and COOH radicals, allow the formation of *at least* two sets of compounds.[8] To the NH_2 group we may tie

[8] The others are not discussed in these pages. That they exist, however, is proved by the too little regarded observation of PAULI that a deaminized protein still combines with sixty percent of the acid with which it combined before deamination.

various acids and so derive the hydrochlorid, hydrobromid, hydriodid, acetate, sulphate or phosphate of the protein; while to the COOH radical may be bound the various bases, thus obtaining the ammonium, potassium, sodium, magnesium or calcium proteinate.

Now how does such chemical treatment of a protein with an acid or an alkali affect its water absorbing qualities? What happens in the case of casein was brought out earlier.[9]

"Neutral" casein absorbs very little water, but as soon as an acid is added, this water absorption is enormously increased. The acid combines with the protein and the acid proteinate thus produced absorbs more water than the "neutral protein." But the effect of any acid varies both with its concentration and its kind. This is at once proof that something more than the mere "presence" of the acid or, as usually assumed, the concentration of its hydrogen ions as yielded upon solution, has increased the hydration capacity of the casein. Obviously neither of these notions can be correct, for neither casein nor any other protein swells equally in different acids of the same C_H or pH; and the acid disappears from the reaction mixture. We can understand these two facts only by saying that the acid *combines* with the protein and that, depending upon the kind of acid in such union, different proteinates are formed, each with its specific capacity for holding water. Thus casein hydrochlorid absorbs more water than the lactate, the lactate more than the acetate and the acetate more than the sulphate; while any living cell subjected to the action of these three acids swells in like order.

When, on the other hand, an alkali is used, the hydration capacity of the casein is also increased. Here again the effect in no wise parallels the hydroxyl ion concentration, the action of every alkali being specific. We can understand this finding only by saying that the alkali has united with the protein to form a series of basic proteinates each of which has its specific power for dissolving water, the caseinates of ammonium, potassium, sodium, magnesium, calcium and barium being progressively weaker in this regard in the order named.

The acid or alkali used in these experiments has, when properly chosen, increased the hydration capacity of the casein. In

[9] See page 134.

this proportion it has produced better colloids of the so-called gel type. What, now, is the nature of this increased hydration or, more generally put, what is the nature of these so-called hydrophilic or lyophilic colloid systems?

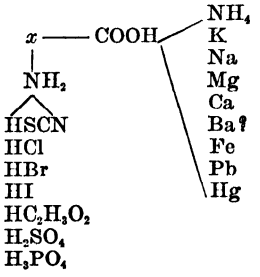
Let us try to find an answer to this question by starting with a fact. If one of the casein gels (say the HCl/casein/water mixture of Fig. 49 or the NaOH/casein/water mixture of Fig. 50) is warmed to 100° in a water bath, the mixture becomes limpid and almost as clear as water. If the physical properties of the system at this high temperature are measured, they are found to approximate those of any so-called true or molecular solution. If the temperature is lowered, these systems at first become opalescent, more viscid, and finally set into solid, semitransparent jellies. The explanation of what happens in this process is illustrated in Fig. 2 (diagrams A and B). Depending upon the temperature alone, every type of system is discoverable from the true solution of the caseinate in the water (at the top) to that of a solution of the water in the caseinate (at the bottom). At first the material is dispersed molecularly or ionically *in* the solvent; in the end, the solvent is "dispersed" in the material.

And where in the diagrams does living matter belong? We have been told (and it is still the majority opinion) that the ground substance in which we are interested lies in the regions A of these diagrams. Actually it lies in the regions Z (or very little above this). *Living matter, including the tissue juices like blood and lymph, is in essence a solution of water in a colloid matrix.* On the other hand the aqueous secretions from the body, like the urine, the sweat and the gastric juice, are essentially water in which some of the constituents of the tissue producing these secretions have been dissolved. These secretions at times contain colloid material, but they are systems which in the main correspond to the zones A in the diagrams (or to the zones lying immediately below this).

What, now, of the "salts" found in the cell? *The salts ashed out of protoplasm are made in the process.* In the living cell they were tied to the protoplasm as so much base and acid. They too are not free but combined with the proteins. Proof of this is found in the fact that fresh animal or vegetable cells do not have a salty taste. And it is only with the greatest difficulty

that a little of the total salts contained in protoplasm can be leached out of cells through treatment with water. Were they "free," as so generally assumed, such extraction should be easy.

If we summarize these findings, cells cease to be droplets of water or droplets of dilute solution in which various (protein, carbohydrate and fat) colloids are "suspended." Cells are, per contra, lyophilic colloid systems in which the water is dissolved in (actually bound to) the colloid material. More specifically put, the solid tissues are in essence conglomerated particles of hydrated proteins (analogous in their structure and behavior to hydrated particles of blood fibrin) while the liquid tissues (the plasma of blood or lymph streams) become "solutions" of hydrated proteins (analogous to the hydrated sols produced when caseinates of various kinds are mixed with water), and the "salts" found in the cells are not "dissolved" merely in this hydrated protein but as acid or base are united with the protein. If from this point of view we revert to protein as a linkage of various amino-fatty-acids and with consideration of its polybasic nature (it is an "amphoteric electrolyte") try to indicate by the *simplest*[10] chemical formula the foundation stone of living matter (the place for carbonic acid being left unfilled) it would look something as follows:



But this is not all. This molecule is not dissolved in water but, on the contrary, is a solvent for water. The water of the living organism must therefore also be tied chemically into this

[10] This linkage of the acids to the free NH_2 groups or of the bases to the COOH groups, as already emphasized, accounts for *less than half* the total neutralization capacity of the proteins (see the observations of Wo. Pauli and M. Hirschfeld: Biochem. Zeitschr. *62*, 245 (1914)). Where and how the remainder is tied is still a matter of hypothesis in organic chemistry.

formula as is the bound water of a crystal in the water of crystallization.

Depending upon the quantity and the kind of each of the acids or bases united with a given protein, we get a series of protein derivatives each with its specific capacity for holding water.[11] In the proteins of the living cell and under physiological circumstances the elements potassium, sodium, magnesium and calcium predominate in the total molecule and hydrochloric, sulphuric, phosphoric and various organic acids (like carbonic). This water-saturated protein molecule is the chemical skeleton in which every physiological activity has its play. The maintenance of this system is physiology and any deviation from it, pathology. The total chemical system may obviously be changed through chemical action occurring either (a) within or (b) without the living cell. From the outside four factors are of great importance—the presence or absence of free water, and the action of acids, alkalies and salts. How do these change the picture of the protein molecule as here drawn? The last three, by chemical addition or substitution, change either the quantity or the quality of the bases or the acids in an upward or downward direction. To add acid or alkali or to shift the radicals upwards is to increase the water-holding capacity of the protein molecule; to subtract acid or alkali or to shift the radicals downwards is to produce an opposite effect. But whatever such change, the essence of living matter, a hydrated base-protein-acid compound, remains.

Under ordinary circumstances the protoplasmic mass is kept in its state of "physiological balance" by being bathed continuously in blood and lymph, these (as mere liquid tissue) being kept of constant composition in their turn by the essential uniformity in the chemical composition of the pabulum furnished them through (a) the water intake, (b) the food intake, and (c) the respiration. Let this environment be altered either through circumstances lying without or within a cell or let therapeutic effort be directed toward such end and the "normal" constitution of the living cell must change. Thus mere application of water to the physiological system "poisons" it as SYDNEY

[11] See page 134.

RINGER[12] early pointed out. The overplus of water acts as a poison because it tends to move protoplasm or the hydrated protein mass illustrated above from some level like Z in Fig. 2 toward a higher one. The protoplasm in other words tends to go into solution *in* the water. Along with this effect, such dilution brings about a hydrolysis. But both the amount of this "solubility" in water and the hydrolysis are stepped down by adding *any* salt to the water. Since, in ordinary circumstances, the elements sodium and chlorine are present in largest amount in the normal protein molecule, a "physiological salt solution" (of NaCl), therefore, proves a less harmful aqueous medium in which to bathe a tissue than water alone. But in this solution and hydrolysis of normal protoplasm more than sodium and chlorine are thus "washed out" of the cell.[13] All the other bases and the other acid elements escape as well. To prevent this, a mixture of several salts (as appears in the solutions of RINGER, HOWELL and COOKE,[14] LOCKE,[15] VAN'T HOFF, etc.) therefore proves to be superior to a plain sodium chlorid solution in the maintenance of the physiological "state" or "activity" of any cell or tissue.

The proteins as they exist in the living cell are not, however, as yet saturated with either acid or alkali, as witness the large quantities of either that may be added without a discoverable shift in their "neutrality." To add either to blood or lymph or tissue may not change the endpoint of an indicator but their hydration is changed by such procedure. Protein hydration or dehydration in other words is a more sensitive "indicator" of the increased or decreased "acid or alkali content" of a biological system than any physicochemical measuring device.

But the quantitative and, what is of equal importance, the qualitative relation of the acids and bases to each other in the protein molecule may be shifted through application to it of any neutral salt. The "therapeutic" administration of various salts (or of acids or of alkalies) represents in essence therefore a *sub-*

[12] SYDNEY RINGER: Jour. Physiol. *4*, 6 (1883); *ibid. 5*, 98 (1884); *ibid. 6*, 154 (1885); *ibid. 11*, 79 (1890); *ibid. 17*, 423 (1895).

[13] See WOLFGANG OSTWALD: Pflüger's Arch. *106*, 568 (1905).

[14] HOWELL and COOKE: Jour. Physiol. *16*, 198 (1893).

[15] LOCKE: Jour. Physiol. *18*, 332 (1895).

stitution therapy in which the administered elements are made to take the place of the acidic or basic radicals normally present in the above formula. We may in this fashion increase the hydration of the total compound by making any lighter metal take the place of a heavier. This is how large doses of ammonium, potassium or even sodium salts work when administered in order to "liquefy" the mucinous secretions of "catarrhally" inflamed surfaces. The sulphocyanates, the iodids and even the chlorids work similarly. A decreased hydration, on the other hand, is obtained by substituting the alkaline earths or the heavier metals for sodium or potassium, or citrate or phosphate for chlorid. In this fashion sodium phosphate and magnesium sulphate or magnesium citrate become powerful dehydrators of the living mass; their entrance into the living mass frees water from its protein combination to "dry" the living cell, while the liberated water becomes a "secretion" from that cell. It is thus that such compounds, through an action upon the *total body,* act and become known as cathartics, diuretics or sudorifics. Still greater dehydration is produced by copper, lead and mercury which through their action upon the proteins come to be known as the "heavy metal poisons."

Recognition of the fact that protoplasm, in its physiological essence, is a base-protein-acid compound and hydrated, that it is, in other words, an "amphoteric electrolyte" not dissolved in water but the solvent for water should help to harmonize the conclusions of a debate a half century old. What is the "reaction" of protoplasm and what do the various methods employed to discover such, really measure?

We may start with the fact that the application in dry form of the commonly employed indicators (as powders, papers or in alcoholic solution) to *normal* tissue (including the blood and lymph) shows these to be "neutral." What is being tested under such circumstances is obviously a solution of inverse type and the indicator methods of the physical chemists function in the (anhydrous) protoplasm as they function in any of the "anhydrous" solutions of inverse type so frequently described.[16]

[16] See pages 113 and 225 or MARTIN H. FISCHER: Chemical Engineer, *27,* 271 (1919); Soaps and Proteins, 77, 229, New York (1921).

This reaction of protoplasm to an indicator does not change perceptibly even when acid or alkali is added, for they unite with the still unsaturated radicals of the protein nucleus to yield compounds which, while richer in acid or alkali (their "acid or alkali content" has been increased) continue to be hydrates and solutions of inverse type. And even when the water content of the total molecule has been allowed to increase (through "swelling" or "edema") it remains bound water and so the basic nature of the system being measured is in no way changed. This explains why in clinical states of edema or in direct acid poisonings even unto death investigators have so rarely been able to demonstrate any change in the C_H or *p*H of blood or tissue.

But utilization of an indicator in *the form here described* in order to discover the reaction of a protoplasmic system is scarcely ever used by the chemists. They begin by *diluting* the system to be measured with four, eight, maybe two hundred parts of water. What this does to the system under measurement must also be clear. The initially, chemically neutral and anhydrous system is made to go into solution in the excess of water and what the indicator now measures is the "hydrogen or hydroxyl ion concentration" *not* of the original hydrate but of the *solution of the hydrate in water* in equilibrium with what may be left of the original phase. Instead of making a physicochemical determination upon a *homogeneous* system, the chemist is making one upon a *heterogeneous*. And what he is measuring are the physicochemical constants of one phase only of the total system. It is as though he were measuring the reaction of a solution of chalk in water against a suspension of that (hydrated) chalk floating in the water. The dangers of assuming that the constants of the *solution* are the constants of the *hydrate* are obvious. In physiology, the cells and the blood are the analogues of the hydrate and the solution of protoplasm in water is represented by *the aqueous secretions from* the body (like the urine or sweat). In these, in states of edema for example (assumed to be a state of increased acid content of the tissues) all students of the question have quite regularly been able to discover an increased titration acidity, an increased C_H or a decreased *p*H.

To use electrical instead of indicator methods increases the reliability of the measurements but it does not alter in any fundamental fashion the question of what is being measured.

In these paragraphs we have made reference most frequently to the significance of such measurement of the hydrogen or hydroxyl ion concentration when made upon "solutions" of chemically neutral proteins or of protoplasm. It does not matter, of course, whether the protoplasm is of plant or animal origin. What we would now like to emphasize is that such hydrogen or hydroxyl determinations carry within themselves the same possibilities for correct or false conclusion when made upon *any* (heterogeneous) hydrated system in equilibrium with a solution of this system in water (like soil, milk products, canned goods or sewage, and the whole range of industrial systems which employ minerals or mineral products, cellulose, gums and starches, water-absorbing alcohols, dyes, inks or soaps and greases).

Regard for the physical chemists' belief that acidity is measured by the concentration of hydrogen ions in any dilute aqueous system and alkalinity by the concentration of the hydroxyl ions (aided by the false assumption that protoplasm, too, because of its high proportion of water, is "nothing but" a dilute solution) has made the modern worker in the biological sciences lay greatest stress upon those methods which measured such values most directly. The alkalinity (or the acidity) of protoplasm was earlier, however, determined by measuring its combining value for a weak acid (like the combining value of blood for carbonic acid[17]) and still earlier for some strong acid (like hydrochloric or sulphuric[18]). As well known, the values arrived at by such different methods yield figures totally different (the "alkalinity" is by the latter methods usually declared to be "higher"). It should be recognized that the statistical findings of all these students are equally correct and that the misunderstanding between them (it continues into the present) arises from the interpretations that they place upon their findings.

[17] F. WALTER: Arch. f. exp. Path. u. Pharm. *7*, 148 (1877); see also FR. KRAUS: *ibid. 26*, 186 (1889).

[18] RUDOLF VON JAKSCH: Klinische Diagnostik, 5 Aufl. 2, 334, Berlin (1901) where references to the classic methods may be found.

When to discover the "alkalinity" of a tissue (including blood or lymph) the material is titrated with any standard acid to some recognized "neutral point" it is obvious that what is really being measured is the combining value for acid of the total system, in other words, its *acid capacity*. The first men who worked on this problem assumed such capacity to lie with certain inorganic constituents found in the tissues (and these in *free* form (as the carbonates and phosphates of sodium, for example)). The studies of KARL SPIRO and WILHELM PEMSEL[19] early showed that the inorganic constituents are insufficient to account for more than a fraction of the total acid (or base) binding capacity and they declared the proteins to play a rôle. Even earlier J. SJÖQVIST,[20] OTTO COHNHEIM,[21] S. BUGARSZKY and L. LIEBERMANN,[22] etc., had demonstrated (the last named by "physicochemical" methods) a direct union of protein with acid (or alkali) so that T. B. ROBERTSON, reverting to the acid combining value of biological systems (like blood) declared something like sixty percent of its total acid held in protein combination. We, ourselves, maintain the fraction to be still higher (almost one hundred percent) since "free" salts are (practically) undiscoverable in normal tissue and the concentrations ordinarily assigned to them are only found after blood has been diluted or "laked" and the more solid tissues subjected to treatment which permits of their hydrolysis. We hold, in other words, that the titration values arrived at are always the product of a double decomposition induced by the added acid (or alkali) acting upon the "normal" base-protein-acid compound which we assume to be the foundation stone of living matter. And this value (depending upon the nature and the "strength" of the acid used for titration, like carbonic, tartaric or sulphuric) is the measure of three variables at least, the combining value for acid (or alkali) of such fraction of the protein as was not yet saturated, plus the combining value represented by the replacement of weaker acids (like carbonic) in the protein molecule by

[19] K. SPIRO and W. PEMSEL: Zeitschr. f. physiol. chem. *26*, 233 (1898).

[20] J. SJÖQVIST: Skand. Arch. f. Physiol. *5*, 277 (1895) where references to such determinations dating back to 1847 (SCHMIDT) may be found.

[21] O. COHNHEIM: Zeitschr. f. Biol. *33*, 489 (1897).

[22] BUGARSZKY and L. LIEBERMANN: Pflüger's Arch. *72*, 51 (1898).

stronger, plus the combining value of the bases (or acids) which through the action of the material used for titration are split off the original protoplasmic mass.

VI. On "Acidosis" and "Alkalosis"

The word "acidosis" was first suggested some fifty years ago as a synonym for "poisoning by acid." The word was coined to cover the state of intoxication produced by F. Walter[23] in animals into which he had injected acids of various kinds. Some years later, when it was discovered that the signs and symptoms described by Walter reappeared in human subjects who were the victims of certain diseases (specifically certain "fevers," cholera and diabetes) these diseases were declared to be states of "acidosis." In straight acid poisoning it does not matter, of course, what is the specific nature of the acid—it is produced as readily by the hydrochloric, sulphuric, phosphoric, or lactic acid which is the product of a "normal" metabolism as by beta-hydroxybutyric or acetoacetic which are deemed to be the products only of a deranged metabolism. The clinical students of the field early fell into grave error. They confused almost at once the *state* of acid poisoning with the possible *mechanisms* resident within the body which might result in such, failing to recognize the *quantitative* nature of poisoning by acid in search for the *qualitative* elements that are likely to appear in certain types of acid poisoning. Thus they early missed the actual "acidoses" incident to heart disease, eclampsia and starvation (because no "abnormal" acids could be isolated from the secretions or tissues of the body) while they declared diabetics and the obese "acidotic" simply because these exhibited in their secretions the products of an abnormal fat chemistry (like beta-hydroxybutyric and acetoacetic). Large numbers of victims showing the presence of such compounds did not, of course, show even the first evidences of any poisoning by acid. For any or all acids may give rise to acid poisoning provided their amount is sufficiently large; on the other hand, even "abnormally" produced acids need not lead to such poisoning when an effective mechanism remains available to neutralize such acid products as

[23] See F. Walter: Arch. f. exp. Path. u. Pharm. *7*, 148 (1877).

formed. For this reason diabetics, fed enough alkali, fail to die of "acidosis" even when their excretion of suboxidized acids is high, for poisoning by acid is essentially a quantitative rather than a qualitative affair. Where does an intoxication with acid attack a cell? *It is in its protein.* But the acid does this not as something which through its C_H or its *p*H "influences" a "colloid" protein, a "micelle" or "colloid behavior" but which as straight acid enters into chemical combination with the cell protein. This protein mass is thereby increasingly hydrated but as a (solid) "solution" of water in the protein shows no change toward any "indicator" that may have been added to the reaction mixture. The "acid content" of the cell or protein has, however, been increased, increased hydration may have been brought about (an edema) but no change worthy of note in the C_H or the *p*H of the total system. Such may be discovered only when water beyond the hydration value of the cell colloids is added, in other words, enough "free" water for some of the acid proteinate to go into solution in it, to be followed by hydrolysis and electrolytic dissociation of the hydrolytic products, and thus a larger concentrate of hydrogen ions than was derivable from the originally more "neutral" or "native" protein. While it is difficult or impossible, therefore, to demonstrate the increased acid content of experimentally produced or clinically recognized states of acid intoxication through the use of indicator or potentiometric methods upon the blood or the body tissues, there is no difficulty in discovering an increased hydrogen ion content of the urine or the sweat, for these represent the collection depots of the free water which the body proteins could not bind and solutions, in consequence, of the protoplasm in water.

Considerations such as these make us define the term "acidosis"—if another definition is needed—as a state in which more than a physiologically "normal" quantity of acid is tied to the protein of the cell. What needs to be remembered is that the first additions of such acid are neutralized by the proteins of the cell. While a cell may, therefore, be poisoned with acid the protoplasm remains in a chemical sense a neutral compound and in physicochemical terms, one which does not show any excess of hydrogen ions. Acid intoxication of a cell betrays

itself, therefore, in changes in its physiological activity and by increased water absorption long before the accepted methods of the dilute solution chemists begin to function.

It is easy to produce an "acidosis" in the living (animal) subject but very hard to produce an "alkalosis." This is because the body's defensive mechanism against the former is more readily exhausted than that against the latter. The living cell is constantly producing acid. Its total is divisible into two halves—a volatile portion represented by carbon dioxid and a fixed portion represented (under normal circumstances) by such acids as hydrochloric, sulphuric and phosphoric. Distinction between the two is of great physiological importance, for while the former is lost without cost to the neutralization machinery of the living organism, the second cannot be lost without dragging along a minimum, at least, of fixed base. It is for this reason that maintenance of normal respiration is of such paramount importance to the living cell, for if the oxidation of its carbon compounds to carbonic acid does not occur, suboxidized intermediates are produced which are non-volatile. To escape their toxic effects the alkali resources of the cell (not of the blood only!) are drawn upon (including not only the much discussed alkaline salts, like the carbonates and basic phosphates, *but the protein of the protoplasm itself!*). It is here where the cell is actually killed. Since these resources are quickly exhausted, *acid* poisoning is the universal product of practically every form of injury to living matter.

Poisoning with alkali (alkalosis) is, on the other hand, difficult to institute. Experimentally, overwhelming doses of alkali must be given and in a short space of time to produce poisonous effects.[24] This is because the amounts of acid produced physiologically are so enormous (to neutralize the twenty-four hour carbonic acid output alone of the adult male requires some two pounds of caustic soda) that it is almost impossible—certainly by any therapeutic means—to bring about an actual poisoning by alkalies. Nevertheless, it is maintained clinically that "alkalosis" exists. The chemical proof for the existence of an actual

[24] MARTIN H. FISCHER: Nephritis, 40, New York (1912) or the later editions.

poisoning by alkali rests on slender grounds. Diagnosis of the state is really made upon the presence of certain clinical signs and symptoms. Wherever there exists a nervous hyperirritability, muscular twitching and a "tetany," especially if such signs are observed after a continuous administration of sodium bicarbonate, after parathyroidectomy or after the persistent vomiting of acid, there are we likely to have the individual's state declared "alkalotic." The fact that, experimentally, enormous quantities of alkali are required to produce poisoning should alone make us dubious regarding the essential origin of the signs and symptoms described but the falsity of their interpretation is proved directly by the fact that certain alkalies only, and not all of them, will produce an "alkalosis." Thus the alkaline salts of sodium or potassium are quite regularly effective, the similar salts of magnesium less so, and those of calcium, not at all. In fact the employment of chalk along with sodium bicarbonate (in gastric ulcer, for example) will suppress the evil effects of the sodium salt as given alone. If, then, we are not dealing with a poisoning by alkalies, what is the nature of the intoxication? *It is an intoxication with light metal salts.*

The matter is easily understood when the physiological effects of the light metal salts are called to mind. W. BIEDERMANN[25] early found that striped muscle begins to twitch in sodium chlorid solutions to which the phosphate, carbonate, bicarbonate, sulphate or hydroxid of sodium had been added while S. RINGER[26] discovered the rhythmic contractions of heart muscle elicited in sodium chlorid to be stopped by calcium chlorid. Such findings have been confirmed by WILLIAM H. HOWELL,[27] J. LOEB[28] and W. D. ZOETHOUT[29] and extended to several other types of physiological conduction, irritability and motion by A. P. MATHEWS.[30]

[25] W. BIEDERMANN: Sitzungsber. d. Wiener Akad. *82*, III (1880); Elektrophysiologie, *92*, Jena (1895).

[26] S. RINGER: Jour. Physiol. *4*, 6 (1883); *ibid. 5*, 98 (1884); *ibid. 6*, 154 (1885); and the later volumes.

[27] W. H. HOWELL: Am. Jour. Physiol. *2*, 47 (1898).

[28] J. LOEB: Festschr. f. Fick, 101, Braunschweig (1899).

[29] W. D. ZOETHOUT: Am. Jour. Physiol. *7*, 199 (1902).

[30] A. P. MATHEWS: Am. Jour. Physiol. *12*, 419 (1905).

What is common in the physiological discovery of all these workers—we forego a discussion of their widely differing hypotheses as to why it happens—is that certain inorganic elements (like sodium, potassium, lithium, etc.) induce a nervous, muscular and motile type of hyperirritability and this *without* any change in "alkalinity"; and that, on the other hand, certain other elements (notably calcium) suppress such effect. On the basis of the considerations that have been outlined in these pages we would, therefore, say that the clinical signs so widely held to be the manifestations of an "alkalosis" are really the effects of poisoning by light metal radicals. "Normal" living matter is a base-protein-acid compound in which are present *several* different bases bearing a certain "normal" quantitative relation to each other (some potassium, more sodium, some calcium and magnesium and some still heavier metals). To subject the compound to the action of any one salt (as in the continuous administration of large quantities of sodium bicarbonate for any "disease" whatsoever) is to displace from normal protoplasm a part of *all* those inorganic elements not contained in the salt being administered. An acid intoxication, for example, tends to crack *all* the bases off the normal cell protein. To meet such intoxication with baking soda alone is to make good the loss of sodium from the cell but not that of any other base. The end result is that of a relative *increase* in the sodium content of the cell. This we hold to be the light metal type of intoxication that goes by the name of "alkalosis." To add to the sodium bicarbonate some magnesium carbonate or chalk is to improve matters and thus to discover the rationale of the finding, that with such a combination of alkalies "alkalosis" does not follow or that the injection of RINGER'S solution in place of "normal saline" into parathyroidectomized individuals stops their "tetany."

VII. EVIDENCE THAT PROTOPLASM IS NOT A DILUTE SOLUTION OF *X* IN WATER

This section summarizes some physiological facts, long known, which prove that protoplasm (including the blood and the lymph of the higher animals) is in no sense a dilute solution but that it is, rather, a concentrated solution and of inverse type, a solu-

tion, in other words, of the water in the protoplasm. Living matter is not in essence the analogue of the regions A in Diagrams A and B of Fig. 2, but, per contra, the analogue of the regions Z.

1. *Protoplasm does not mix with water nor with any kind of dilute solution.* An ameba does not dissolve in its pond water, nor a fish in the sea; a man may go in swimming or be rained upon and not "dissolve." The same is true, of course, of all forms of vegetable life. It is true even of the fragments of living forms. Soup meat keeps its body even when indefinitely stewed in water, and the same holds for the vegetables. Blood and lymph will mix with water, but the "shadows" of their cellular constituents remain, and what happens to the "plasma" we shall see shortly.

2. *Fragments of the living mass, be they cells, tissues or organs, "swell" when thrown into water.* This is due to the hydrophilic colloids they contain and is exhibited by the separate hydrophilic colloids which may be derived from living plants or animals. Dilute solutions do not "swell' when poured into water but are simply lost.

3. *Protoplasm follows no known law of the dilute solution chemist.* No cell obeys the laws of osmotic pressure; and no dissolved substance (even when chemically non-reactive with any constituent of the living mass) passes into or out or through a living cell at a rate identical with its diffusion velocity in water.

4. *The concentration in which any material may be dissolved in protoplasm is always different from that in which it may be dissolved in an equivalent volume of water (it is either lower or higher than anticipated).* This is the so-called "selective" absorption of protoplasm. Dynamic study of this phenomenon has yielded us those endless studies of biological "permeability" familiar to every worker in physiology.

5. *Protoplasm shows an unwontedly high resistance to the passage of an electric current.* The electrical resistance of any dilute solution assumed to be comparable with protoplasm is low. A salt solution, for example, made by dissolving in an equivalent volume of water the salts ashed out of protoplasm, shows a resistance of several ohms with standard electrodes; the protoplasm itself, several hundred. This fact cannot

be explained except by saying that (a) protoplasm is not an aqueous solution, or that (b) there are (practically) no free salts in protoplasm to act as conductors. We shall see that both these statements are correct.

6. *Protoplasm does not lend itself easily to any measurement of its acidity or alkalinity* (its C_H or *p*H, for example). This is perfectly easy in the case of the ordinary aqueous solutions, by gas chain, indicator or potentiometric means. Yet such determinations as made upon cells are hardly known; those made on vacuole contents, saps and cellular extracts are questioned as to their validity by the observers themselves; those common measurements which have been made upon blood and lymph have too often been made only after dilution of these materials with water, or after dialysis, or under other circumstances which change completely the character of the original liquids.

7. *The course of chemical reactions in water is, in general, in the direction of analysis; the course of these same reactions in protoplasm, in the direction of synthesis.* Not only complex organic compounds but simple inorganic salts tend to break down "spontaneously" into simpler forms when in contact with water; complex carbohydrates dissociate into simpler sugars, fats go "rancid," proteins decompose into simpler complexes, and many inorganic salts "hydrolyze." Within the living cell such hydrolysis is enormously stepped down; and the ready *synthesis* of proteins, fats and carbohydrates from their simpler building stones by cells stands out as *the* characteristic of the living mass.

The next section will adduce the evidence which proves that protoplasm is a solution of inverse type and that while it shows none of the characteristics of a solution of x in water (like phenol or quinolin in water) it shows all those of a solution of water in x (like water in phenol or quinolin).

VIII. Proof that Protoplasm is a Solution of Water in X

The following paragraphs (numbered like those of the preceding section) show that the physicochemical characteristics of a solution of water in x are those which reappear whenever protoplasm is examined for its properties.

1. If equal volumes of phenol and water (see Figs. 3 and 12) or quinolin and water are left together until equilibrium is estab-

lished, the *hydrated phenol or quinolin phase will not mix with the water phase.* If shaken, the hydrated phenol or quinolin breaks into droplets and these may then be observed to float about in the water phase as so many amebae or white blood cells. In other words, hydrated phenol or hydrated quinolin does not mix and lose itself in water any more than does the primitive animal or vegetable cell, or a fish. Protoplasm is, therefore, comparable to a solution of water in phenol or quinolin; while the secretions from the body (like urine, sweat or gastric juice), are comparable to a solution of phenol in water.

2. *Phenol or quinolin, brought in contact with water, "swells."* If equal volumes of water and phenol are mixed, the two solutions that result are, in the end, unequal in volume. As water dissolves in the phenol, the volume of the phenol increases. It "swells" some twenty-eight to thirty percent at 22° C. This is the analogue of the amount of water which a cell will absorb under "normal" circumstances. But the degree to which phenol "swells" may be altered under conditions identical with those which make living cells take up more or less water. Just as alkalies make isolated cells or proteins swell, so do they increase the amount of water absorbed by phenol. The effect may be seen in Fig. 3. With every increase in the alkali content of the phenol/water system, there is a progressive increase in the amount of "swelling" shown by the hydrated phenol phase. Acids do not increase the water absorbing capacity of phenol. But all neutral salts decrease it, depending upon (a) their concentration and (b) their kind. Progressive increase in the concentration of any salt about the hydrated phenol leads to increasing shrinkage (just as progressive increase in the concentration of the salt in any solution surrounding the living cell leads to its progressively greater shrinkage). But at the same "osmotic" concentration, potassium, sodium and calcium salts are increasingly effective in the order named (just as a potassium salt leads to less dehydration of a living cell than an equally concentrated sodium or calcium salt). But non-electrolytes, like the various monatomic alcohols, do not bring about such decrease in the volume of the hydrated phenol phase as do salts. They quite regularly increase its volume, and in mounting value

with increase in the concentration of the added alcohol. This is the analogue of the behavior of various non-electrolytes upon the living cell, in which also urea, for example, at any "osmotic" concentration leads only to increased swelling on the part of the cell, while the various anesthetics (like the alcohols) (see Fig. 12) act similarly or at least fail to dehydrate a cell at "osmotic" concentrations in which the salts are very effective.

In the case of quinolin/water systems, only about ten percent of water is absorbed by the quinolin phase, and neither acids nor alkalies perceptibly change this amount. All salts however decrease this "swelling," and increasingly with increase in their concentration. Various monatomic alcohols show no such action, but, on the contrary, increase the amount of water taken up by the quinolin.

3. *We imagine that few scientific workers would be willing to declare a drop of hydrated phenol or of quinolin to be an "osmotic" system. And yet such droplets are "plasmolyzed" or "plasmoptyzed," depending upon the nature and the concentration of the salt solution surrounding them, as is any living cell under similar conditions.* But if a drop of hydrated phenol or quinolin is discovered to behave in these regards like a living cell, why continue the assumption that the latter must be an osmotic system? No living cell is known which follows the mathematical laws of osmotic pressure. But if the living cell is made a solution of water in x the requirement that it shall follow the laws of osmotic pressure in its hydration and dehydration obviously ceases to be of any moment. Protoplasm as a system comparable to a solution of water in phenol or in quinolin is dehydrated through salts, for example, by laws which have nothing to do with the laws of osmotic pressure. And the surprise so commonly registered when various non-electrolytes (the monatomic alcohols especially) fail to dehydrate living cells even when employed in proper "osmotic" concentrations disappears. The same materials fail similarly to dehydrate hydrated phenol or quinolin.

No physical chemist, probably, would make out hydrated phenol or quinolin to be a "solution" comparable to, or a mere continuation (in "concentrated" form) of the dilute solu-

tion of either of these materials *in* water. He would not therefore expect these systems to register osmotic pressures comparable to the concentration of the phenol or the quinolin in them. And yet this is the view which is taken of protoplasm when the cell is conceived of as an osmotic machine.

4. Just as the solubility of any third material is different in protoplasm from its solubility in an equivalent volume of water (it dissolves in either a lower or a higher concentration) so *the solubilities of any third material are different in the two types of solution, phenol or quinolin in water, and water in phenol or quinolin.*

When phenolated water and hydrated phenol are in contact with each other, the latter phase will take up certain substances better than the former, or vice versa. The analogy to what has been observed in "permeability" studies on living cells is again great. The hydrated phenol is quickly "permeable" to the most varied dyes (Nile blue sulphate, neutral red, methyl red, methyl violet, methyl green) and will practically exhaust the water phase in a few hours. Other substances (like eosin or iodin) will pass in less quickly and less completely. All the salts (so often held by various biological students incapable of entering or leaving the uninjured living cell) enter the hydrated phenol phase either very slowly or not at all. Ferric chlorid, cupric acetate, cerium sulphate (or their hydrolytic products) all enter the phenol phase, but with decreasing facility; chromium chlorid, chromium sulphate, cobaltous chlorid, nickel chlorid, seem to remain entirely in the aqueous phase. Of "colloid" substances, infusorial earth concentrates in the aqueous phase, bone black in the phenol phase.

With slight variation, the same may be said of the distribution of these materials between the phases, quinolined water and hydrated quinolin. Neutral red, Nile blue sulphate, methyl violet, methyl green and iodin all leave the aqueous phase of a quinolin/water system to concentrate in the hydrated quinolin phase. Eosin, methylene blue and methyl red color both phases. Different salts like nickel chlorid, chromium chlorid, copper acetate and iron chlorid remain in the aqueous phase; towards these the hydrated quinolin is practically "impermeable."

5. The unexpectedly high electrical resistance that all observers have found to be characteristic of protoplasm is to be attributed to the fact that it is not a dilute solution of an electrolyte. It is not to be compared with a five per cent solution of phenol in water, for example, which is a good conductor of electricity, but with the concentrated mixture of phenol with water which we have here called hydrated phenol or a solution of *water in phenol. This mixture, in spite of its higher content of "electrolyte" does not show itself to be a proportionately better conductor, but one infinitely worse.* It registers a resistance many hundred times that of the dilute solution of phenol in water. The same is true when quinolined water is compared with hydrated quinolin (or a solution of sulphuric acid in water with one of water in sulphuric acid) or when solutions of various colloids in water gel to solutions of water in the colloid. The latter subject receives detailed discussion in a succeeding section.[31]

6. *We are ignorant of the true "acidity" or "alkalinity" of cells, tissues, organs and blood simply because the schemes which have been devised for their measurement have all been derived from the study of dilute aqueous solutions; and living matter is not such.* Protoplasm is not a dilute solution but something different. We might as justly try to use gas chain, indicator or potentiometric methods to determine the acidity of crystallized glacial acetic acid, or the alkalinity of calcium acetate crystallized with its water of crystallization, as to make similar tests upon a kidney, a liver or a pancreas. To express it in another way, protoplasm is a solvent for an "indicator," for example, different from water. And just as we cannot use the color exhibited by an indicator dissolved in a hydrocarbon, an alcohol or an ether to tell us what is its reaction, even so must great care be used in deducing the C_H or pH of protoplasm from the stray color that an indicator assumes when dissolved in it; or to make the analogy with "aqueous solutions" more close, when the indicator is dissolved in the anhydrid of a pure acid or in the acid itself in "concentrated" form.

7. If protoplasm is a solution of water in x, and especially if it is true that this water is united to the protoplasm as water is

[31] See page 228.

bound to an anhydrid or to a crystal in water of crystallization, it follows that *there is no free water in protoplasm* (including the blood and the lymph). Proof to support this conclusion has been brought many times before.[32] It means that protoplasm is not only not a dilute aqueous solution but that (in spite of its sixty to ninety percent of water) it is essentially *anhydrous.* It follows by corollary that *all reactions occurring in this medium occur in the absence of water* and it is to be expected therefore that their course, the equilibrium finally reached, and the products of the reaction, must be totally different from those obtaining when this same reaction takes place in an aqueous medium. The reactions which take place in the alimentary tract, for example, must therefore run differently, since they occur in what is essentially an aqueous medium, from the same reactions when they take place in the (anhydrous) tissues or the blood or the lymph. This matter finds discussion later.[33]

IX. On the So-called "Permeability" of Living Cells

We return in this section to a somewhat more detailed discussion of the "permeability" exhibited by cells and to point out the relation which the experiments detailed in this volume bear to the total problem. The question of the "permeability" of "cell membranes" and more recently, of "protoplasm" in general, has been the subject of extensive experimental inquiry and debate for many years past. The discussion of no idea in modern biology has yielded a more voluminous literature and none has rested more content in its contradictions and in its complete failure to place itself properly in the fields of chemistry or physics. It is unnecessary to go into details regarding the findings and the fantasies of the various workers. They may be found in the papers and texts of such workers as E. Overton,[34]

[32] Martin H. Fischer: Œdema, 184, New York (1910); Kolloidchem. Beihefte, *2*, 308 (1911); ibid, *3*, 387 (1912); etc.

[33] See page 230.

[34] E. Overton: Vierteljahresschr. Naturforsch. Ges. Zürich, *40*, 1 (1895), ibid., *44*, 88 (1899); Z. Physik. Chem., *22*, 189 (1897); Pflüger's Arch., *92*, 115 (1902); ibid., *92*, 261 (1902); Nagel's Handbuch d. Physiol. 2, 2te Hefte, 744 (1907).

H. J. HAMBURGER,[35] RUDOLPH HÖBER,[36] J. F. MCCLENDON,[37] E. NEWTON HARVEY,[38] and W. J. V. OSTERHOUT.[39] No one may attempt a critical analysis of these studies without a feeling of dismay. And yet in spite of many contradictions as to observations but more especially as to deductions, some fundamental harmonies remain.

1. The first permeability studies were built upon the osmotic concept of the living cell as originally advanced by PFEFFER and DE VRIES. The living cell was, according to their notion, a saccule of fluid encompassed by a semipermeable membrane—a membrane, in other words, impermeable to all dissolved substances but readily permeable to water. A first observation to disturb this concept of the cell was made by these authors themselves when they noted that various dissolved substances would diffuse into cells and precipitate the tannin contained therein. This fact (with many others which we have adduced ourselves and which were touched upon above[40]) led us early to deny the existence of semipermeable membranes about cells.[41] How then are we to understand the biological studies of "permeability" which have so long been interpreted through the assumption that some kind of membrane, "semipermeable," "lipoid" or "plasmatic," exists about cells when this concept is done away with? The answer is simple.

We have repeatedly emphasized that the hydrophilic colloid (especially one protein in nature, like a particle of fibrin) is possessed of all the powers of taking up and giving off water

[35] H. J. HAMBURGER: Osmotischer Druck and Ionenlehre, *1*, 202, Wiesbaden (1902).

[36] R. HÖBER: Physikal. Chem. d. Zelle und d. Gewebe, 5te Aufl., 367 and 404, Leipzig (1922) as well as the older editions.

[37] J. F. MCCLENDON: Pop. Science Monthly, 568 (1915); Am. J. Physiol., *38*, 163 1915); ibid., *38*, 173 (1915); Am. J. Surg., Anesthesia Supplement, *35*, 104 (1921).

[38] E. NEWTON HARVEY: Yearbook No. 10, Carnegie Institution, 128 (1910); J. Exp. Zool., *10*, 507 (1911); Am. J. Physiol., *31*, 335 (1913).

[39] W. J. V. OSTERHOUT: Injury, Recovery and Death, Philadelphia, (1922).

[40] See page 193.

[41] MARTIN H. FISCHER: Am. J. Physiol., *20*, 330 (1907); Pflüger's Arch., *124*, 69 (1908); ibid., *125*, 99 (1908); ibid., *127*, 1 (1909); ibid., *127*, 46 (1909); Œdema, New York (1910).

shown by the living cell, and that it has at the same time all the powers of taking up and giving off dissolved substances which are characteristic of living matter.[42] All this occurs, of course, without the need of assuming that the hydrated colloid mass has a membrane about it which differs in any way from the rest of the fibrin flake. Our more recent studies[43] have shown that such a protein mass, combined with acids and alkalies or salts and saturated with water (and comparable in this form with the foundation material constituting the cell) is in essence a system comparable to water-dissolved-in-phenol. It is this water-dissolved-in-phenol system which, when subjected to the action of alkalies or of salts, "swells" and "shrinks," shows, in other words, the biological phenomenon of plasmoptysis and plasmolysis (too commonly still explained on an "osmotic" basis) just as does a hydrophilic colloid (a protein) or a living cell.

But this system shows also the "strange" phenomena of "permeability" to dissolved substances so characteristic of living matter. When phenolated water and hydrated phenol are in contact with each other, the latter phase will take up certain substances better than the former, or vice versa. And here the analogy to what has been observed in permeability studies on living cells is again great. The hydrated phenol is quickly "permeable" to the most varied dyes and will practically exhaust an aqueous phase of these materials in a few hours; other substances pass in less quickly and less completely; and all the salts (so often held by various biological students incapable of entering or leaving the uninjured living cell) enter the hydrated phenol phase either very slowly or not at all.[44]

2. A second method of studying the "permeability" of "cell membranes" or of protoplasm has been by electrical means. Living tissues register a certain resistance to passage of the electrical current, and this resistance may be markedly changed (usually reduced) through injury, or the action of acids and alkalies, heat, anesthetics, etc. As a matter of fact the experi-

[42] MARTIN H. FISCHER: Œdema, 200, New York (1910); Œdema and Nephritis, 3rd Ed., 206, 318, 367, 640, New York (1921).

[43] MARTIN H. FISCHER: Science, *48*, 143 (1918); Soaps and Proteins, 205, 228, New York (1921).

[44] See page 112.

ments described above on hydrated phenol and quinolin were devised to show, if possible, that the peculiarities which living matter shows to the passage of an electric current through it may be readily understood as soon as it is remembered that the cell is not, as so long conceived, a dilute solution of x-in-water but one of water-in-x.

The first fact which strikes the student investigating the electrical resistance of cells or biological fluids is its height.[45] In spite of the conclusion, for example, that a "physiological" salt solution (say a 0.7% or 0.9% NaCl solution) is one which "osmotically" is supposed to be comparable with the "cell contents" (a material usually conceived of as a solution of the salts found in protoplasm "dissolved" within the cellular water) the former will register, with a standard pair of electrodes, only 1/5 to 1/35 the electrical resistance of uninjured cells, muscle juice, lymph, blood, egg white or egg yolk. This old biological truth can be understood only by denying to the salts found in protoplasm any large existence in uncombined form[46] or by concluding that the cell is a different sort of solvent for these salts than is water. Experimental facts support both conclusions. The high electrical resistance characteristic of living protoplasm cannot be observed in solutions of the type phenol-dissolved-in-water but only in those of the type water-dissolved-in-phenol.

Under the heading of changes in electrical resistance evidenced by living cells when subjected to intoxication, injury or environmental change, the following has been noted by all observers. The electrical resistance of protoplasm is reduced through the action of acids or alkalies. In similar fashion, acids and alkalies are most powerful in decreasing the electrical resistance of hydrated phenol. But potassium hydroxid reduces the electrical resistance of protoplasm more than an equally concentrated sodium hydroxid and this more than calcium hydroxid. Hy-

[45] See the many observations covering this point beginning with W. ROTH: Zentr. f. Physiol., *11*, 271 (1897); BUGARSZKY and TANGL: ibid., *11*, 297 (1897); Pflüger's Arch., *73*, 531 (1898); G. N. STEWART: Zentr. f. Physiol., *11*, 332 (1897); J. Physiol., *24*, 356 (1899); Am. J. Physiol., *49*, 233 (1919).

[46] See in this connection MARTIN H. FISCHER: Soaps and Proteins, 228, New York (1921).

drated phenol behaves similarly. The electrical resistance of living cells is also reduced through the action of any single salt but less effectively than by acids or alkalies. This too is characteristic of the electrical resistance of hydrated phenol. In its action upon a cell any single salt may, however, prove itself more "poisonous" at certain concentrations than at others. The salt will act similarly upon hydrated phenol. The absolute difference in physiological effect exhibited by different salts when employed in comparable concentrations is also repeated in the case of hydrated phenol. Finally, the physiological antagonism between different salts (the ability of a divalent radical, for example, to counteract the electrical reducing effects of a univalent one) may also be observed upon hydrated phenol. Even the effects of certain non-electrolytes in reducing the electrical resistance of protoplasm (as that of the anesthetic alcohols) may be rediscovered in hydrated phenol systems.

In these remarks the analogy has been pointed out between the "permeability behavior" of living cells and that half of the mutually soluble system phenol/water which is *not* a dilute solution of phenol in water but one of the water in phenol. The analogy carries through and for the similar phase of all other mutually soluble systems that have been studied namely, quinolin/water, soaps/water and various proteins/water.

X. Synthesis in Living Matter

The evidence presented, compels the conclusion that neither living matter nor any fraction of it is to be thought of primarily as a dilute solution or as anything approximating such a system. It is, rather, a protein to which the salts have been bound chemically (fundamentally as a base-protein-acid compound) and *in* which the water has then been "dissolved" (or to which the water has been bound as a hydrate). This four part affair is to our minds the fundamental unit of the living mass. The relation of the carbohydrates and the fats to this primary system is a matter that has been ignored—in large part at least they are "emulsified" or "suspended" in this hydrated living mass—because experiment shows that the primary effects of all agencies

which influence any physiological reaction are upon the protein constituents of the living substance.

If the conclusion is accepted that all the water of the living mass is held in bound form it leads to an important corollary. The chemical reactions which occur in living matter must occur in a medium far different from ordinary water. *Living matter is normally a practically anhydrous medium; the chemical reactions characteristic of the normal life of the cell occur in an anhydrous medium and their course and products must, in consequence, be entirely different from the course and products of these same reactions occurring in and familiar to us from study of the ordinary aqueous solution.*

The physiologist and the biochemist are always astonished at the remarkable powers of *chemical synthesis* exhibited by living protoplasm. While the chemist, by the use of acids and alkalies, or heat and water, or through the gentler action of those fragments of the living mass which he calls ferments, has been able to break up the complex organic proteins, carbohydrates and fats into their simpler building blocks, he has had great difficulty in resynthesizing these materials into their original forms. Yet living matter does this with the greatest ease. A beefsteak with bread and butter, which melts in the lumen of the intestine into amino acids, simple sugars and fatty acids and glycerin and is thus "absorbed," is so rapidly resynthesized into protein, glycogen and fat by the living cells that the building blocks can scarcely be discovered in the blood or lymph which carries the absorbed meal away.

It was a great step forward when A. Croft Hill, Kastle and Loevenhart, Hanriot and their successors first showed us that the ferments were capable of catalyzing not only an analysis but also a synthesis. It must be admitted, however, that in test-tube experiments this "reversible action of the ferments" has never proved itself to be very great so far as the synthesis half of the problem is concerned. *The reason for this resides in a fact, we believe, which chemistry has overlooked: nature always makes her analysis in an aqueous medium and her synthesis in an anhydrous one. The agencies which digest a meal in the alimen-*

tary tract work in the presence of much free water; the same agencies work in the body substance in the presence of none.

The importance of such arrangement may be illustrated in the synthesis of a soap from a fatty acid and a hydroxid. To accomplish our end suitable quantities of fatty acid and alkali are mixed with very little water. As chemical combination takes place and soap is formed this product binds the water (both that originally present and that produced in the reaction) so that in the end 100 percent of hydrated soap is formed—synthesis is, in other words, carried to completion. If now merely water is added to the reaction mixture, analysis begins—we say that the soap hydrolyzes into alkali and free fatty acid. At proper concentration this reaction, too, tends to be complete. With a medium amount of water, either reaction "tends toward an equilibrium"—in other words, to a mixture of soap with alkali and fatty acid.

Again, iron and iodin combine directly to iron iodid. If this reaction is carried out in water, nothing but an indeterminate reddish-green mixture of a little iron iodid, much iron hydroxid, and hydriodic acid, is obtained. Add cane sugar to the original mixture (which combines with the water to make "syrup") and a clear solution of ferric iodid in the hydrated sugar is obtained —in other words, with water, hydrolysis and analysis; without water, synthesis.

Over what route in general does the organic chemist accomplish his syntheses? The fact should be noted by the physical chemists who interest themselves in the problems of biological chemistry—the anhydrous one.

To illustrate the matter, we may look at the problem of fat synthesis in the body. Fat production is ester production. Suppose we look at the approved method of producing an ester like ethyl butyrate. If ethyl butyrate is mixed with a considerable quantity of water, nothing seems to happen, for ethyl butyrate is hardly soluble in water. But if shaking is continued for a little time, the ethyl butyrate collar becomes perceptibly thinner. This is explained by saying that the ethyl butyrate hydrolyzes into ethyl alcohol and butyric acid, both of which are readily soluble in water. Such hydrolysis of the ester is greatly

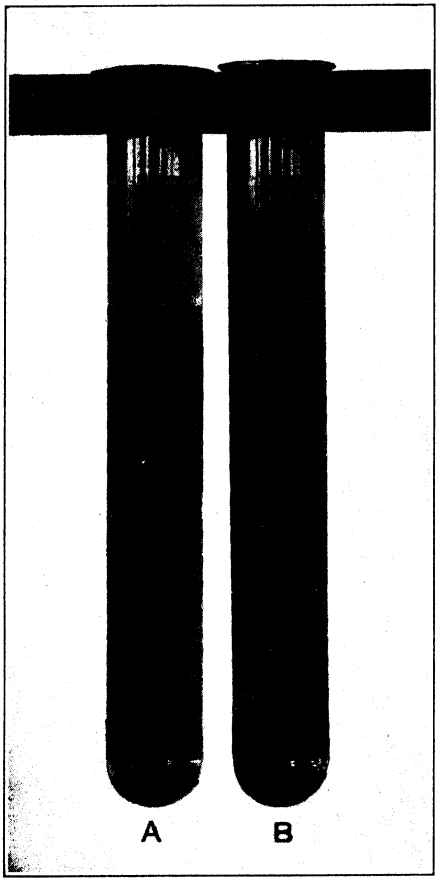


FIG. 84

hastened by adding any acid, like sulphuric acid; and this total change has been the subject of much careful study by the physical chemists. We deal here with the decomposition of an ester in the presence of much water (the analogue of the digestion of a "fat" into fatty acid and alcohol in the lumen of the gut).

Let us look now at the obverse of this experiment. Molar equivalents of butyric acid and absolute ethyl alcohol (17.6 gms. butyric acid + 9.2 gms. ethyl alcohol) are mixed together. If this mixture is merely allowed to stand—provided *absolute* ethyl alcohol has been used—a considerable synthesis of ethyl butyrate takes place within several days; to explain the matter, we say that the synthesis is made possible not only because we started with anhydrous materials, but because the reaction was kept anhydrous through the taking up of the water formed in the process of synthesis by the absolute alcohol present. We can hurry along this reaction by adding any third substance which will take up this water as quickly as formed. Concentrated sulphuric acid works very well. Suppose the ethyl alcohol-butyric acid mixture is divided between two tubes; if a few drops of concentrated sulphuric acid are added to the one, and the contents of the two tubes are then immediately diluted with water, the picture shown in Fig. 84 may be observed. The original mixture mixes with the water to yield a water-clear fluid (Tube B of Fig. 84), but the mixture treated with the sulphuric acid has a thick collar of ethyl butyrate at the top (Tube A of Fig. 84). A one hundred percent synthesis of a "fat" may thus be accomplished in a very few minutes.

In place of the butyric acid in this experiment, there may be employed any other water soluble fatty acid (through valeric) and in place of ethyl alcohol, any other water soluble alcohol (through butyl), while instead of sulphuric acid there may be used any one of several other "driers," like phosphorus pentoxid, calcium chlorid, or any colloid capable of maintaining its water-holding powers in the mixture. The essential thing is the removal of the "free" water present in the original mixture, or formed chemically.[47] This explains why some synthesis is ob-

[47] The same is true of nitration and sulphonation. In nitration, the sulphuric acid of the nitric-sulphuric acid mixture used does not appear in the end products but serves to keep the reaction mixture anhydrous; while in sulphonation, the excess of sulphuric acid used serves the same end.

tained when butyric acid with absolute alcohol alone is employed, especially when an excess of the alcohol is used, and the enormous speeding up of this reaction if a strong dehydrating agent is introduced into the reaction mixture to take up the water as formed by the union of the fatty acid with the alcohol.

XI. On Pharmaceutical Preparation

The view here emphasized, that protoplasm is a practically anhydrous medium and that, in consequence, the hydrolytic cleavage of its hydrolyzable compounds is under natural circumstances inhibited (their synthesis, on the other hand, favored) explains and finds large support in the empiric practices long followed by the pharmaceutical chemist both in the extraction of such compounds for medicinal use and their preservation in unchanging form afterwards. The "teas" of witch doctors and Indian squaws, and the more scientific "infusions" of the modern pharmacist, as aqueous extracts of various plant protoplasms, show a high tendency to "spoil"—they either "decompose" of themselves or they become "infected" with moulds or other forms of organic life which hasten such "spontaneous" decomposition. In general, all these plant extracts are mixtures of some higher carbohydrates, various essential oils and other esters, organic acids in combination with stronger bases, alkaloids, either pure or combined with acid, and various dyes and glucosids. The tendency of all such compounds to suffer decomposition when "dissolved" in water (especially hot water) needs no comment. The change, in the main, is a set of hydrolyses. To overcome this decomposition the pharmaceutical chemist has employed two schemes—he has either dried down his original infusion to obtain a more solid "extract" or he has used some other "solvent" for water, namely, alcohol, glycerin or sugar. What he does by such methods—to revert again to our terminology—is to assure himself of an anhydrous medium, or, when water still enters the picture, to add something to combine with this water to the end that his total mixture may again become "anhydrous."

We will not pursue the subject further in the instance of the pharmacopeial spirits, tinctures or fluid extracts of various

plant tissues, for, independently of the country of their issue, very few of these carry less than seventy percent of ethyl alcohol or some other alcohol (like glycerin). In such a medium any decomposition due to hydrolysis is enormously stepped down (see the next paragraphs). The pharmaceutical preparations of greater interest to us are those in which water is still present in considerable fraction but where hydrolysis is nevertheless largely absent owing to the addition of sugar. These are the "elixirs" and the "syrups"; the former still carrying a considerable fraction of alcohol plus sugar, the latter, essentially only sugar. The number of "syrups" that appears in the pharmacopeias of the United States, Great Britain, France or Germany is very large. Some of these are the "odors, flavors and dyes" extracted from various plant structures (like orange peel, bitter almond or wild cherry) and "dissolved" in sugar-water (usually cane sugar but sometimes the monosaccharids represented by honey, molasses or invert sugar) while others are the chemically better defined materials represented by various salts. Under the latter head appear the syrups of ferrous iodid or hydriodic acid, of calcium lactophosphate or iron phosphate with quinin and strychnin, the compound syrup of sodium, potassium, calcium and iron hypophosphite, etc.

The value of sugar in "stabilizing" the "solutions" of all these materials has been known for a century. We would like to emphasize the reason for such stabilization. *The sugar combines with the water present in all these mixtures yielding a "syrup"; but such syrup is not a solution of sugar in water but one of inverse type,* in other words, a hydrate in the sense in which we have used this word. The materials present in the pharmaceutical preparation are still "soluble" in this sugar-water but they do not hydrolyze in it. The truth of this general statement finds support in another observation, that of DUPASQUIER[48] (1838) who found that ferrous iodid could be kept from decomposing by uniting the water of its solution not only to a sugar but to any of the hydrophilic colloids represented by the vegetable "gums." And the same fact is brought out in everyday kitchen practice when the housewife secures against

[48] DUPASQUIER: cited in the U. S. Dispensatory.

decomposition by water, time or the invasion of microörganisms, her fruits and vegetables or their expressed juices by the simple expedient of "concentrating" them, the addition of sugar, or the production within them, or through addition to them, of water-absorbing colloids (pectin, agar-agar).[49]

This influence of saccharose and dextrose (and of ethyl alcohol and glycerin) as water-binding substances upon the hydrolysis of an ester (methylacetate) has received quantitative study by JOSEPH L. DONNELLY.[50] Using an electrical method for determining the degree of hydrolytic cleavage he found the addition of either sugar to inhibit such cleavage and about equally at the same concentration and temperature. The degree of inhibition was increased with every increase in the amount of sugar added to the reaction mixture, a 1/10 molar concentration cutting down the rate, as compared with pure water, some thirty percent, a 2/10 molar over fifty percent and a 3/10 molar over seventy-five percent. Ethyl alcohol is somewhat weaker in this action and glycerin decidedly stronger. DONNELLY explains the effects through union of the water with the materials added and thus the removal of the water from the components of the hydrolytic reaction.

XII. CONCLUDING REMARKS

The discussion in these last pages began with an inquiry into the nature of the physicochemical system that constitutes protoplasm. Protoplasm carries a high fraction of water but this is related to the rest of the materials that make up protoplasm not as the water of a dilute solution but as the water found in a hydrophilic colloid. In other words, protoplasm holds its water by virtue of its colloid content (the proteins chiefly) and the amount of water thus held under physiological or pathological circumstances is determined by the chemical nature of the col-

[49] WILLIAM B. WHERRY has built up a whole concept of "immunity" to infection on such basis. The organisms that cannot break down the water-holding colloids of an invaded tissue can get no free water for their growth and so can live (if at all) only saprophytically. Organisms pathological for a host are always splitters of protein and the like which, by such method, not only set water free but secure the degradation products of protoplasm for their further life and multiplication.

[50] JOSEPH L. DONNELLY: Kolloid-Zeitschr. *38*, 165 (1926).

loids produced by such circumstances. When, for example, the "neutral" (protein) colloids of a cell are acidified or alkalinized, new proteinates are produced possessed of a different (usually greater) water-holding capacity. In the terms of pathology, an edema has been produced. When, on the other hand, "normal" proteinates are treated with calcium, iron or mercury, another set of derivatives is produced, possessed of a lower water-holding capacity, which action applied to living cells leads to their abnormal dryness.

When definition of the nature of such water-holding capacity is attempted, it is found to be comparable to the way in which phenol or quinolin holds (or "dissolves") water. It is not comparable to the relation which exists between water and dissolved substance in the ordinary solution. This explains why the physicochemical laws (the dilute solution laws) derived from study of the latter type of systems do *not* apply to protoplasm (the laws of diffusion, osmotic pressure, electrolytic dissociation, reaction rate, equilibrium, reaction to indicators, etc.).

Protoplasm is *not,* as generally held, a solution of x-in-water but a system of inverse type, a solution of water-in-x. The secretions from protoplasm (like the urine, sweat or gastric juice) on the other hand, approximate the type, protoplasmic substance dissolved in water. Protoplasm may be compared to a solution of water in phenol or quinolin or soap; its aqueous secretions, to a solution of phenol or quinolin or soap in water.

Just as water is not "free" in protoplasm, but an integral part of the living mass, so also are its "salts." The salts generally said to be found in normal protoplasm have really been produced in the process of its analysis. They were originally bound chemically to the proteins as acid or base. Proof for this is found in both physiological and chemical fact. Thus fresh animal or plant tissues do not taste like the aqueous solutions of the electrolytes that may be extracted from them; and the electrical resistance of such tissues is so high that it can be understood only by saying (a) that the electrolytes are not free in protoplasm and (b) that protoplasm is not a solvent for them comparable to an equivalent volume of water. Both these propositions are true. Whatever electrolytes may exist "free" in protoplasm and merely "dissolved" in it may be declared a "solution" of

these materials but they are dissolved not in water but in a hydrated biocolloid.

Dissolved substances do not enter cells nor protoplasm as they enter an ordinary aqueous solution, because cells are not such. Salts, non-electrolytes, dyes, etc., enter protoplasm as they enter a solution of water-in-*x* (water-in-phenol, water-in-quinolin, water-in-soap, etc.).

Further proof that protoplasm and the body fluids (like the blood and lymph) are not dilute solutions is given by their behavior toward indicators. They react toward these not like solutions of the type phenol, quinolin, soap or protein in water, but like solutions of water *in* these materials. Concentrated mixtures of (chemically neutral) soap with water (solutions of water in soap) are neutral to an indicator like phenolphthalein, while more dilute ones (solutions of soap in water) are intensely alkaline. This is true also of alkaline gelatinates or alkaline caseinates and may be demonstrated directly upon their biological analogues, blood plasma and tissue juices. The same behavior may be observed even in those apparently simple systems familiar to the physical chemist and represented, for instance, by various highly concentrated acids or their anhydrids (solutions, in our terminology, of water in the acid).

If what has been said is accepted as correct, it follows that progress in the physicochemical or colloid-chemical analysis of protoplasm will be possible only as it ceases its still too prevalent effort to apply by force the dilute solution laws, including the laws of osmotic pressure, to biological phenomena. A better and more fruitful period will be upon us when attention is fixed upon the behavior of what we must call, for lack of a better name, *solutions of inverse type,* under which heading there will reappear a large number of those solutions which the chemist has called "concentrated." When we have discovered their laws, when we have familiarized ourselves with the physicochemical and colloid-chemical behavior of systems of the type water-dissolved-in-*x,* we shall find ourselves possessed also of the laws which govern the behavior of protoplasm under physiological and pathological circumstances.

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